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L48 ANSWER 1 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 2001:203166 HCAPLUS
TI Addressing genomics with **combinatorial chemistry**: Mixture-based solution phase **libraries**
AU **Shipps, Gerald W., Jr.**; Rosner, Kristin E.; Makara, Gergely; Curran, Patrick
CS Department of Chemistry, **NeoGenesis** Drug Discovery, Cambridge, MA, 02139, USA
SO Abstr. Pap. - Am. Chem. Soc. (2001), 221st, ORGN-660
CODEN: ACSRAL; ISSN: 0065-7727
PB American Chemical Society
DT Journal; Meeting Abstract
LA English
AB To address the opportunities of genomics we have developed a versatile, expansive **combinatorial chem.** platform that we term **NeoMorph**.- The **chem.** uses both soln. & solid phase strategies to create defined, mass-encoded mixts. of diverse, medicinally relevant small mols. that are **screened** against **proteins** of interest.

L48 ANSWER 2 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 2001:199212 HCAPLUS
TI On validating 3-D diversity methods: Introducing total pharmacophore diversity
AU Makara, Gergely; **Wintner, Edward**
CS Department of Chemistry, **NeoGenesis** Drug Discovery, Cambridge, MA, 02139, USA
SO Abstr. Pap. - Am. Chem. Soc. (2001), 221st, CINF-055
CODEN: ACSRAL; ISSN: 0065-7727
PB American Chemical Society
DT Journal; Meeting Abstract
LA English
AB Validation of pharmacophore derived metrics for quantifying mol. diversity usually involves comparison of 2D and 3D techniques. Such studies have often made the rather surprising and counterintuitive conclusion: 2D fingerprints elucidate exptl. data more reliably than 3D methods. This

presentation details several pitfalls that should be avoided in constructing sets of mols. to be used in diversity validation. Mols. erroneously expected to be similar can have a major impact on the obsd. performance of diversity methods and are compared by 2D Unity and Total Pharmacophore Diversity (ToPD) fingerprints. ToPD, a new distance-based 3D method is also demonstrated to consistently and significantly outperform 2D binary fingerprints in different validation tests. The ToPD algorithm can be used for rapid evaluation of diversity in large **screening libraries** or generation of focused **libraries** as well as **ligand**-based virtual **screening**.

L48 ANSWER 3 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:267987 HCAPLUS
DN 133:53164
TI Quantized Surface Complementarity Diversity (QSCD): A Model Based on Small Molecule-Target Complementarity
AU **Wintner, Edward A.**; Moallemi, Ciamac C.
CS **NeoGenesis Inc., Cambridge, MA, 02139, USA**
SO J. Med. Chem. (2000), 43(10), 1993-2006
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
CC 1-3 (Pharmacology)
AB A model of mol. diversity is presented. The model, termed "Quantized Surface Complementarity Diversity" (QSCD), defines mol. diversity by measuring mol. complementarity to a fully enumerated set of theor. target surfaces. Mol. diversity space is defined as the mol. complement to this set of enumerated surfaces. Using a set of known test compds., the model is shown to be biol. relevant, consistently scoring known actives as similar. At the resoln. of the model, which examines mols. "quantized" into 4.24 .ANG. cubic units and treats four points of specific energetic complementarity, the min. no. of compds. needed to fully cover mol. diversity space up to vol. 1070 cubic .ANG. is estd. to be on the order of 24 million mols. Most importantly, QSCD allows for individual points in diversity space to be filled by direct modeling of mol. libraries into detailed 3D templates of shape and functionality.
ST quantized surface complementarity diversity QSCD model drug target
IT Conformation
Drug design
Molecular recognition
Structure-activity relationship
(quantized surface complementarity diversity (QSCD), a model based on small mol.-target complementarity)
RE.CNT 50
RE
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L48 ANSWER 4 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:220916 HCAPLUS
DN 133:159520
TI Chemical **ligands**, genomics and drug discovery
AU Lenz, G. R.; Nash, H. M.; **Jindal, S.**
CS **NeoGenesis, Cambridge, MA, USA**
SO Drug Discovery Today (2000), 5(4), 145-156
CODEN: DDTOFS; ISSN: 1359-6446
PB Elsevier Science Ltd.
DT Journal; General Review
LA English
CC 1-0 (Pharmacology)
AB A review with 45 refs. The sequencing of the human genome and numerous pathogen genomes has resulted in an explosion of potential drug targets. These targets represent both an unprecedented opportunity and a technol. challenge for the pharmaceutical industry. A new strategy is required to initiate small-mol. drug discovery with sets of incompletely characterized, disease-assocd. **proteins**. One such strategy is the early application of **combinatorial chem**. and other technologies to the discovery of bioactive small-mol. **ligands** that act on candidate drug targets. Therapeutically active **ligands** serve to concurrently validate a target and provide lead structures for downstream drug development, thereby accelerating the drug discovery process.
ST review genome drug discovery **combinatorial chem**
IT **Combinatorial chemistry**
Drug design
Drug targeting
(**chem. ligands**, genomics and drug discovery)
RE.CNT 45
RE
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L48 ANSWER 5 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:451260 HCAPLUS
DN 131:87511
TI Method for producing mass-coded **combinatorial libraries**
IN **Nash, Huw M.; Birnbaum, Seth; Wintner, Edward A.; Kalghatgi, Krishna; Shipps, Gerald; Jindal, Satish**
PA **Neogenesis, Inc., USA**
SO PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07B061-00
ICS B01J019-00; G01N033-50
CC 21-2 (General Organic Chemistry)
Section cross-reference(s): 1, 6, 34
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9935109	A1	19990715	WO 1999-US24	19990104
	W: JP				

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
US 6207861 B1 20010327 US 1998-24592 19980217 <--
EP 1045819 A1 20001025 EP 1999-900730 19990104
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
PRAI US 1998-70456 P 19980105
US 1998-24592 A 19980217
WO 1999-US24 W 19990104

AB The present invention provides a method for producing a mass-coded **combinatorial library** comprising a set of compds. having the general formula X(Y)n, where X is a scaffold, each Y is, independently, a **peripheral** moiety, and n is an integer greater than 1. The method comprises selecting a **peripheral** moiety **precursor** subset from a **peripheral** moiety **precursor** set. The subset includes a sufficient no. of **peripheral** moiety **precursors** that at least about 50 distinct combinations of n **peripheral** moieties derived from the **peripheral** moiety **precursors** in the subset exist. The subset of **peripheral** moiety **precursors** is selected so that at least about 90% of all possible combinations of n **peripheral** moieties derived from the subset have a **mol. mass** sum which is distinct from the **mol. mass** sums of all of the other combinations of n **peripheral** moieties. The method further comprises contacting the **peripheral** moiety **precursor** subset with a scaffold **precursor** which has n reactive groups. Methods of use of the mass-coded **combinatorial library** produced by this method for identifying a **ligand** to a particular biomol. are also disclosed.

ST mass coded **combinatorial library** prepn

IT **Combinatorial library**
Molecular weight
(method for producing mass-coded **combinatorial libraries**)

RE.CNT 7

RE
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L48 ANSWER 6 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:684249 HCAPLUS
DN 130:51971
TI **Combinatorial libraries** in solution: polyfunctionalized core molecules
AU **Wintner, Edward A.**; Rebek, Julius, Jr.
CS Skaggs Institute for Chemical Biology, The Scripps Research Institute, La Jolla, CA, 92037, USA
SO Comb. Chem. (1997), 95-117. Editor(s): Wilson, Stephen R.; Czarnik, Anthony W. Publisher: Wiley, New York, N. Y.
CODEN: 66VLAI
DT Conference; General Review
LA English
CC 21-0 (General Organic Chemistry)
AB A review with 28 refs.
ST **combinatorial library** soln review
IT **Combinatorial library**
(prepn. of **combinatorial libraries** in soln.)

RE.CNT 51

RE
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L48 ANSWER 7 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:568789 HCAPLUS
DN 129:189669
TI Process for creating molecular diversity
IN Rebek, Julius, Jr.; Carell, Thomas; **Wintner, Edward A.**
PA Massachusetts Institute of Technology, USA
SO PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07B061-00
ICS C07D311-82
CC 34-2 (Amino Acids, Peptides, and Proteins)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 9835923 A1 19980820 WO 1998-US2812 19980213
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
AU 9861638 A1 19980908 AU 1998-61638 19980213
PRAI US 1997-799874 19970214
WO 1998-US2812 19980213
AB Methods for forming **combinatorial libraries** and the **libraries** produced thereby are provided. A plurality of core mols. (9,9-dimethylxanthene-2,4,5,7-tetraacid chloride or 1,3,5,7-cubanetetraacid chloride) are reacted with a plurality of different tool mols. (an **amino acid**, nucleoside, nucleotide, carbohydrate, lipid, or their analogs) to form a **library** of mols. having non-naturally occurring mol. diversity. The **libraries** are useful for identifying lead compds. which modulate the functional activity of a biol. mol.
ST **amino acid** deriv **combinatorial library**
IT **Combinatorial library**
(formation of **combinatorial libraries**)
IT **Amino acids**, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(formation of **combinatorial libraries**)
IT 108-91-8, Cyclohexylamine, reactions 2393-23-9, 4-Methoxybenzylamine 19814-75-6, 9,9-Dimethylxanthene 68858-20-8 98930-01-9 103213-32-7 109425-51-6 161980-55-8
RL: RCT (Reactant)
(formation of **combinatorial libraries**)
IT 165465-27-0P 171176-59-3P 171176-60-6P 171176-61-7P 171176-64-0P 171176-65-1P 171176-66-2P 171176-67-3P 171176-68-4P 211870-67-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(formation of **combinatorial libraries**)
IT 46339-96-2P 166034-32-8P 171176-62-8P 171176-63-9P 171176-70-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(formation of **combinatorial libraries**)

L48 ANSWER 8 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:277671 HCAPLUS
DN 128:289517
TI Rapid characterization of **combinatorial libraries** using electrospray ionization Fourier transform ion cyclotron resonance mass spectrometry
AU Fang, A. S.; Vouros, P.; Stacey, C. C.; Kruppa, G. H.; Laukien, F. H.; **Wintner, E. A.**; Carell, T.; Rebek, J., Jr.
CS Department of Chemistry, Barnett Institute, Northeastern University, Boston, MA, 02115, USA
SO Comb. Chem. High Throughput Screening (1998), 1(1), 23-33
CODEN: CCHSFU; ISSN: 1386-2073
PB Bentham Science Publishers
DT Journal
LA English
CC 80-5 (Organic Analytical Chemistry)
Section cross-reference(s): 22
AB The relatively new field of **combinatorial chem.** has enabled researchers to create large mixts. of compds. that can be **screened** for leads in developing potential drug candidates. The new synthetic method has also created a need for better procedures to analyze the complex mixts. that are generated. The immediate goal in most cases is to verify the synthetic procedure and to det. the purity and completeness of the **library** sample before binding studies are initiated. The authors report here a method to rapidly characterize

small-mol. combining a core mol. bearing two acid chloride functionalities with various **amino acids** to generate **libraries** of 36, 78 and 120 components. Using electrospray ionization Fourier transform ICR mass spectrometry (ESI-FTICR-MS) the authors were able to identify 70-80% of the **library** components. All samples were analyzed as mixts. by direct infusion without chromatog. sepn. Also, nominally isobaric components could be resolved and identified through exact mass assignments without tandem mass spectrometry. ESI-FTICR-MS is a rapid and convenient tool for the characterization of small-mol. **libraries**. The method is esp. useful for the anal. of larger **libraries** that contain many nominally isobaric components and impurities.

ST **combinatorial library** Fourier ICR mass spectrometry; ion cyclotron resonance MS **combinatorial library**

IT **Combinatorial library**
Fourier transform ion cyclotron resonance mass spectrometry
(rapid characterization of **combinatorial libraries** using electrospray ionization Fourier transform ion cyclotron resonance mass spectrometry)

IT 178916-23-9
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(132060265rapid characterization of **combinatorial libraries** using electrospray ionization Fourier transform ion cyclotron resonance mass spectrometry)

IT 616-34-2, Glycine methyl ester 2812-46-6 3017-32-1 4299-70-1, L-Tryptophane methyl ester 10332-17-9, L-Methionine methyl ester 13211-31-9, L-Valine-tert-butyl ester 13795-73-8 16874-06-9 16874-17-2 21691-50-9 21691-53-2, L-Leucine-tert-butyl ester 24205-25-2 25456-86-4, L-Asparagine-tert-butyl ester 35146-32-8 48067-24-9 52616-82-7 80745-10-4
RL: RCT (Reactant)
(building block in rapid characterization of **combinatorial libraries** using electrospray ionization Fourier transform ion cyclotron resonance mass spectrometry)

IT 166034-31-7
RL: RCT (Reactant)
(core mol. in rapid characterization of **combinatorial libraries** using electrospray ionization Fourier transform ion cyclotron resonance mass spectrometry)

IT 178915-00-9 178915-02-1 178915-03-2 178915-04-3 178915-05-4
178915-06-5 178915-07-6 178915-08-7 178915-09-8 178915-10-1
178915-11-2 178915-12-3 178915-13-4 178915-14-5 178915-15-6
178915-16-7 178915-17-8 178915-18-9 178915-19-0 178915-20-3
178915-30-5 178915-31-6 178915-32-7 178915-33-8 178915-34-9
178915-35-0 178915-37-2 178915-38-3 178915-39-4 178915-40-7
178915-41-8 178915-42-9 178915-43-0 178915-45-2 178915-46-3
178915-47-4 178915-48-5 178915-50-9 178915-51-0 178915-52-1
178915-54-3 178915-55-4 178915-56-5 178915-57-6 178915-58-7
178915-59-8 178915-60-1 178915-61-2 178915-62-3 178915-64-5
178915-65-6 178915-66-7 178915-67-8 178915-81-6 178915-83-8
178915-87-2 178915-88-3 178915-92-9 178915-93-0 178915-94-1
178915-95-2 178915-96-3 178915-97-4 178915-98-5 178916-00-2
178916-01-3 178916-02-4 178916-03-5 178916-05-7 178916-06-8
178916-07-9 178916-08-0 178916-09-1 178916-10-4 178916-11-5
178916-12-6 178916-14-8 178916-15-9 178916-16-0 178916-17-1
178916-20-6 178916-21-7 178916-22-8 178916-24-0 178916-25-1
178916-26-2 178916-27-3 178916-29-5 178916-30-8 178916-32-0
178916-35-3 178916-36-4 178916-37-5 178916-39-7 178916-40-0
178916-43-3 178916-45-5 178916-46-6 178916-47-7 178916-48-8
178916-49-9 178916-50-2 178916-52-4 178916-53-5 178916-54-6
205806-37-7 205806-38-8 205806-39-9 205806-40-2 205806-41-3
205806-42-4 205806-43-5 205806-44-6 205806-45-7 205806-46-8
205806-47-9 205806-48-0 205806-49-1 205806-50-4 205806-51-5
205806-52-6 205806-53-7 205806-54-8 205806-55-9 205806-58-2
205806-64-0 205806-67-3 205806-70-8 205806-72-0 205806-74-2
205806-76-4 205806-77-5 205806-78-6 205806-79-7

RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(rapid characterization of **combinatorial libraries** using electrospray ionization Fourier transform ion cyclotron resonance mass spectrometry)

L48 ANSWER 9 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:222703 HCAPLUS
DN 129:4516
TI I. solution-phase **combinatorial chemistry**: the activated core approach. ii. porphyrin-based small molecule receptors
AU **Shipps, Gerald W., Jr.**
CS Massachusetts Institute of Technology, Cambridge, MA, USA
SO (1997) 5973 pp. Avail.: UMI, Order No. DA0598715
From: Diss. Abstr. Int., B 1998, 58(11), 5973
DT Dissertation
LA English
CC 26-7 (Biomolecules and Their Synthetic Analogs)
AB Unavailable
ST soln phase **combinatorial chem**; porphyrin receptor
IT **Combinatorial chemistry**
(using porphyrin-based small mol. receptors in the activated core approach of soln.-phase **combinatorial chem**.)
IT Porphyrins
RL: MSC (Miscellaneous)
(using porphyrin-based small mol. receptors in the activated core approach of soln.-phase **combinatorial chem**.)

L48 ANSWER 10 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:710500 HCAPLUS
DN 128:43412
TI Synthesis and **screening** of small molecule libraries active in binding to **DNA**
AU **Shipps, Gerald W., Jr.**; Pryor, Kent E.; Xian, Jun; Skyler, David A.; Davidson, Eric H.; Rebek, Julius, Jr.
CS The Skaggs Institute for Chemical Biology and Department of Chemistry, The Scripps Research Institute, La Jolla, CA, 92037, USA
SO Proc. Natl. Acad. Sci. U. S. A. (1997), 94(22), 11833-11838
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
CC 1-3 (Pharmacology)
Section cross-reference(s): 27, 34
AB Five synthetic tetraurea **combinatorial libraries** of 2,080 components each were **screened** as mixts. for inhibition of **DNA** binding to two transcription factors. Rapid, soln.-phase synthesis coupled to a gel-shift assay led to the identification of two compds. active at a 5- to 10-.mu.M concn. level. The likely mode of inhibition is intercalation between **DNA** base pairs. The efficient deconvolution through sublibrary synthesis augurs well for the use of large mixts. of small, nonpeptide mols. in biol. **screens**.
ST tetraurea **combinatorial library screening** **DNA** binding; xanthine tetraurea **combinatorial library DNA** binding
IT Structure-activity relationship
(**DNA**-binding; synthesis and **screening** of small mol. tetraurea libraries active in binding to **DNA** in relation to structure)
IT **Combinatorial library**
Drug screening
Intercalation (**nucleic acid**)
(synthesis and **screening** of small mol. tetraurea **libraries** active in binding to **DNA** in relation to structure)
IT **DNA**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

(synthesis and **screening** of small mol. tetraurea libraries active in binding to **DNA** in relation to structure)

IT 199858-52-1P 199858-53-2P 199858-54-3P 199858-55-4P 199858-56-5P 199858-57-6P 199858-58-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(intermediate; synthesis and **screening** of small mol. tetraurea libraries active in binding to **DNA** in relation to structure)

IT 16874-17-2 165465-27-0 166034-32-8 178915-23-6
RL: RCT (Reactant)
(reactant; synthesis and **screening** of small mol. tetraurea libraries active in binding to **DNA** in relation to structure)

IT 199858-59-8P 199858-60-1P 199858-61-2P 199858-62-3P 199858-63-4P 199858-64-5P 199858-65-6P 199858-66-7P 199858-67-8P 199858-68-9P 199858-69-0P 199858-70-3P 199858-71-4P 199858-72-5P 199858-73-6P 199858-74-7P 199858-75-8P
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and **screening** of small mol. tetraurea libraries active in binding to **DNA** in relation to structure)

L48 ANSWER 11 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:175128 HCAPLUS
DN 126:168806
TI High speed, automated, continuous flow, multi-dimensional molecular selection and analysis
IN **Jindal, Satish**; Regnier, Fred E.; Williams, Kevin; Afeyan, Noubar B.; Paliwal, Sandeep; Evans, David; Pingali, Aruna
PA Perseptive Biosystems, Inc., USA
SO PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM G01N030-46
CC 9-3 (Biochemical Methods)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9701755	A2	19970116	WO 1996-US10929	19960626
	WO 9701755	A3	19970306		
	W: JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 835446	A2	19980415	EP 1996-923455	19960626
	R: DE, GB				
	JP 11509314	T2	19990817	JP 1996-504548	19960626
PRAI	US 1995-518		19950626		
	WO 1996-US10929		19960626		

AB The invention provides novel methods for **screening** a sample to select a **ligand** to a target of interest and for obtaining information about the **ligand** and its binding characteristics. Specifically, the claimed multi-dimensional methods involve combining a soln. of heterogeneous **ligands** with the target of interest to **screen** the **ligands** on the basis of one or more binding characteristics. **Ligands** having the first binding characteristic bind to the target of interest thereby to form a target/**ligand** complex. The complex then optionally is sepd. from the unbound components using any of a variety of sepn. techniques, e.g., size exclusion. At least one of the complex or unbound components then is introduced to a second "dimension". The second dimension is capable of sepg. components based upon a second binding characteristic. One then elutes the **ligand** having the desired being characteristics. **Screening** of a synthetic **peptide combinatorial library** using an antibody against .beta.-endorphin as a target is described.

ST **peptide combinatorial library** chromatog

immobilization; **ligand** target mol binding antibody
IT **Combinatorial library**
Ion-exchange chromatography
Mass spectrometers
(high speed, automated, continuous flow, multi-dimensional mol. selection and anal.)
IT **Proteins** (general), biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(high speed, automated, continuous flow, multi-dimensional mol. selection and anal.)
IT **Peptides**, biological studies
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(high speed, automated, continuous flow, multi-dimensional mol. selection and anal.)
IT IgG
RL: PUR (Purification or recovery); PREP (Preparation)
(high speed, automated, continuous flow, multi-dimensional mol. selection and anal.)
IT Antibodies
RL: RCT (Reactant)
(high speed, automated, continuous flow, multi-dimensional mol. selection and anal.)
IT Biopolymers
RL: RCT (Reactant)
(high speed, automated, continuous flow, multi-dimensional mol. selection and anal.)
IT Endotoxins
RL: RCT (Reactant)
(high speed, automated, continuous flow, multi-dimensional mol. selection and anal.)
IT Immobilization (molecular)
RL: RCT (Reactant)
(high speed, automated, continuous flow, multi-dimensional mol. selection and anal.)
IT **Ligands**
RL: RCT (Reactant)
(high speed, automated, continuous flow, multi-dimensional mol. selection and anal.)
IT **Protein** A
RL: RCT (Reactant)
(high speed, automated, continuous flow, multi-dimensional mol. selection and anal.)
IT **Protein** G
RL: RCT (Reactant)
(high speed, automated, continuous flow, multi-dimensional mol. selection and anal.)
IT 11028-71-0P, Con A
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(high speed, automated, continuous flow, multi-dimensional mol. selection and anal.)
IT 60617-12-1, .beta.-Endorphin
RL: RCT (Reactant)
(high speed, automated, continuous flow, multi-dimensional mol. selection and anal.)

L48 ANSWER 12 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:555064 HCAPLUS
DN 125:269747
TI Use of a **peptide library** to characterize differential **peptide** binding specificities of bacterial and mammalian Hsp70
AU Williams, K. P.; Evans, D. M.; Rosenberg, S.; **Jindal, S.**
CS PerSeptive Biosystems Inc., Framingham, MA, USA
SO Tech. Protein Chem. VII, [Symp. Protein Soc.], 9th (1996), Meeting Date 1995, 57-64. Editor(s): Marshak, Daniel R. Publisher: Academic, San

Diego, Calif.
CODEN: 63GTAE
DT Conference
LA English
CC 9-16 (Biochemical Methods)
AB A **peptide library** contg. a random mixt. of **peptides** of different lengths and sequences and having an affinity for mammalian hsp70 or its bacterial counterpart, **Dna** K, was **screened**. The results showed that although mammalian and bacterial hsp70 are highly conserved **proteins**, they differ in their specificity for binding **peptides**. The **screening** approach should be useful for obtaining **ligands** that differentiate between closely related targets.
ST **peptide** binding specificity bacterial mammalian hsp70
IT **Proteins**, specific or class, properties
RL: PRP (Properties)
(characterization of differential **peptide** binding specificities of bacterial and mammalian Hsp70)
IT **Proteins**, specific or class
RL: PRP (Properties)
(hsp 70, characterization of differential **peptide** binding specificities of bacterial and mammalian Hsp70)

L48 ANSWER 13 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:367060 HCAPLUS
DN 125:81189
TI Application of capillary electrophoresis-electrospray ionization mass spectrometry in the determination of molecular diversity
AU Dunayevskiy, Yuriy M.; Vouros, Paul; **Wintner, Edward A.**; **Shipps, Gerald W.**; Carell, Thomas; Rebek, Julius, Jr.
CS Dep. Chem., Northeastern Univ., Boston, MA, 02115, USA
SO Proc. Natl. Acad. Sci. U. S. A. (1996), 93(12), 6152-6157
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
CC 9-16 (Biochemical Methods)
AB By capillary electrophoresis coupled online to electrospray ionization MS, a **library** of theor. 171 distributed xanthene derivs. was analyzed. The method allowed the purity and makeup of the **library** to be detd.: 160 of the expected compds. were found to be present, and 12 side-products were also detected in the mixt. Due to the ability of capillary electrophoresis to sep. analytes on the basis of charge, most of the xanthene derivs. could be resolved by simple capillary electrophoresis-MS procedures even though 124 of the 171 theor. compds. were isobaric with .gtoreq.1 other mol. in the mixt. Any remaining unresolved peaks were resolved by MS/MS expts. The method shows promise for the anal. of small **combinatorial libraries** with <1000 components.
ST xanthene deriv capillary electrophoresis mass spectrometry
IT **Combinatorial library**
(application of capillary electrophoresis-electrospray ionization mass spectrometry in detn. of mol. diversity of xanthene derivs.)
IT Electrophoresis and Ionophoresis
(capillary, application of capillary electrophoresis-electrospray ionization mass spectrometry in detn. of mol. diversity of xanthene derivs.)
IT Mass spectrometry
(electrospray-ionization, application of capillary electrophoresis-electrospray ionization mass spectrometry in detn. of mol. diversity of xanthene derivs.)
IT 92-83-1D, Xanthene, derivs.
RL: ANT (Analyte); ANST (Analytical study)
(application of capillary electrophoresis-electrospray ionization mass spectrometry in detn. of mol. diversity of xanthene derivs.)
IT 110-18-9, N,N,N',N'-Tetramethylethylenediamine 19814-75-6, 9,9-Dimethylxanthene

RL: RCT (Reactant)
(application of capillary electrophoresis-electrospray ionization mass spectrometry in detn. of mol. diversity of xanthene derivs.)

IT 178915-00-9P 178915-01-0P 178915-02-1P 178915-03-2P 178915-04-3P
178915-05-4P 178915-06-5P 178915-07-6P 178915-08-7P 178915-09-8P
178915-10-1P 178915-11-2P 178915-12-3P 178915-13-4P 178915-14-5P
178915-15-6P 178915-16-7P 178915-17-8P 178915-18-9P 178915-19-0P
178915-20-3P 178915-21-4P 178915-22-5P 178915-23-6P 178915-24-7P
178915-25-8P 178915-26-9P 178915-27-0P 178915-28-1P 178915-29-2P
178915-30-5P 178915-31-6P 178915-32-7P 178915-33-8P 178915-34-9P
178915-35-0P 178915-36-1P 178915-37-2P 178915-38-3P 178915-39-4P
178915-40-7P 178915-41-8P 178915-42-9P 178915-43-0P 178915-44-1P
178915-45-2P 178915-46-3P 178915-47-4P 178915-48-5P 178915-49-6P
178915-50-9P 178915-51-0P 178915-52-1P 178915-53-2P 178915-54-3P
178915-55-4P 178915-56-5P 178915-57-6P 178915-58-7P 178915-59-8P
178915-60-1P 178915-61-2P 178915-62-3P 178915-63-4P 178915-64-5P
178915-65-6P 178915-66-7P 178915-67-8P 178915-68-9DP, N-trityl deriv. 178915-69-0DP, N-trityl deriv. 178915-70-3DP, N-trityl deriv.
178915-71-4DP, N-trityl deriv. 178915-72-5DP, N-trityl deriv.
178915-73-6DP, N-trityl deriv. 178915-74-7DP, N-trityl deriv.
178915-75-8DP, N-trityl deriv. 178915-76-9DP, N-trityl deriv.
178915-77-0DP, N-trityl deriv. 178915-78-1DP, N-trityl deriv.
178915-79-2DP, N-trityl deriv. 178915-80-5P 178915-81-6P
178915-82-7P 178915-83-8P 178915-84-9P 178915-85-0P 178915-86-1P
178915-87-2P 178915-88-3P 178915-89-4P 178915-90-7P 178915-91-8DP, N-trityl deriv. 178915-92-9P 178915-93-0P 178915-94-1P
178915-95-2P 178915-96-3P 178915-97-4P 178915-98-5P 178915-99-6P
178916-00-2P 178916-01-3P 178916-02-4P 178916-03-5P 178916-04-6DP, N-trityl deriv. 178916-05-7P 178916-06-8P 178916-07-9P
178916-08-0P 178916-09-1P 178916-10-4P 178916-11-5P 178916-12-6P
178916-13-7P 178916-14-8P 178916-15-9P 178916-16-0P 178916-17-1P
178916-18-2P 178916-19-3P 178916-20-6P 178916-21-7P 178916-22-8P
178916-23-9P 178916-24-0P 178916-25-1P 178916-26-2P 178916-27-3P
178916-28-4P 178916-29-5P 178916-30-8P 178916-31-9P 178916-32-0P
178916-33-1DP, N-trityl deriv. 178916-34-2P 178916-35-3P
178916-36-4P 178916-37-5P 178916-38-6P 178916-39-7P 178916-40-0P
178916-41-1P 178916-42-2DP, N-trityl deriv. 178916-43-3P
178916-44-4P 178916-45-5P 178916-46-6P 178916-47-7P 178916-48-8P
178916-49-9P 178916-50-2P 178916-51-3P 178916-52-4P 178916-53-5P
178916-54-6P 178916-55-7P 178916-56-8DP, N-trityl deriv.
178916-57-9P 178916-58-0P 178916-59-1P 178916-60-4P 178916-61-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(application of capillary electrophoresis-electrospray ionization mass spectrometry in detn. of mol. diversity of xanthene derivs.)

IT 178916-62-6P 178916-63-7P 178916-64-8P 178916-65-9P 178916-66-0P
178916-67-1P 178916-68-2P 178916-69-3P 178916-70-6P 178916-71-7P
178916-72-8P 178916-73-9P 178916-74-0P 178916-75-1P 178916-76-2P
178916-77-3P 178916-78-4P 178916-79-5P 178916-80-8P 178916-81-9P
178916-82-0P 178916-83-1P 178916-84-2P 178916-85-3P 178916-86-4P
178916-87-5P 178916-88-6P 178916-89-7P 178916-90-0P 178916-91-1P
178916-92-2P 178916-93-3P 178916-94-4P 178916-95-5P 178916-96-6P
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178917-02-7P 178917-03-8P 178917-04-9P 178917-05-0P 178917-06-1P
178917-07-2P 178917-08-3P 178917-09-4P 178917-10-7P 178917-11-8P
178917-12-9P 178917-13-0P 178917-14-1P 178917-15-2P 178917-16-3P
178917-17-4P 178917-18-5P 178917-19-6P 178917-20-9P 178917-21-0P
178917-22-1P 178917-23-2P 178917-24-3P 178917-25-4P 178917-26-5P
178917-27-6P 178917-28-7P 178917-29-8P 178917-30-1P 178917-31-2P
178917-32-3P 178917-33-4P 178917-34-5P 178917-35-6P 178917-36-7P
178917-37-8P 178917-38-9P 178917-39-0P 178917-40-3P 178917-41-4P
178917-42-5P 178917-43-6P 178917-44-7P 178917-45-8P 178917-46-9P
178917-47-0P 178917-48-1P 178917-49-2P 178917-50-5P 178917-51-6P
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178917-57-2P 178917-58-3P 178917-59-4P 178917-60-7P 178917-61-8P
178917-62-9P 178917-63-0P 178917-64-1P 178917-65-2P 178917-66-3P
178917-67-4P 178917-68-5P 178917-69-6P 178917-70-9P 178917-71-0P

178917-72-1P 178917-73-2P 178917-74-3P 178917-75-4P 178917-76-5P
178917-77-6P 178917-78-7P 178917-79-8P 178917-80-1P 178917-81-2P
178917-82-3P 178917-83-4P 178917-84-5P 178917-85-6P 178917-86-7P
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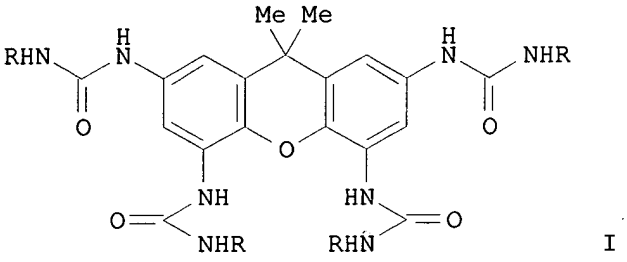
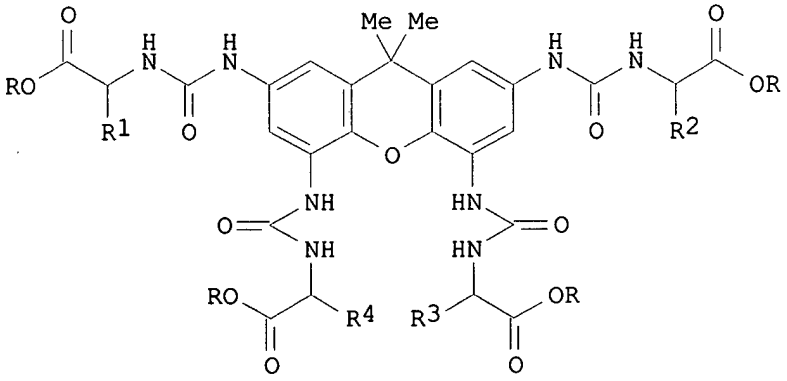
178917-97-0P 178918-98-1P 178917-99-2P 178918-00-8P 178918-01-9P
178918-02-0P 178918-03-1P 178918-04-2P 178918-05-3P 178918-06-4P
178918-07-5P 178918-08-6P 178918-09-7P 178918-10-0P 178918-11-1P
178918-12-2P 178918-13-3P 178918-14-4P 178918-15-5P 178918-16-6P
178917-17-7P 178918-18-8P 178918-19-9P 178918-20-2P 178918-21-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(application of capillary electrophoresis-electrospray ionization mass spectrometry in detn. of mol. diversity of xanthene derivs.)

L48 ANSWER 14 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:362832 HCAPLUS
DN 125:168591
TI Solution-phase generation of tetraurea libraries
AU **Shipps, Gerald W., Jr.**; Spitz, Urs P.; Rebek, Julius, Jr.
CS Department Chemistry, Massachusetts Institute Technology, Cambridge, MA, 02139, USA
SO Bioorg. Med. Chem. (1996), 4(5), 655-657
CODEN: BMECEP; ISSN: 0968-0896
DT Journal
LA English
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 27
GI



I



II

AB Libraries of tetraureas tethered to a rigid core were assembled. This simple, soln.-phase methodol. generated a defined, anticipated distribution of compds. These conclusions were supported by synthesizing pure (homo) tetraurea xanthenes and by HPLC anal. of small 'micro libraries'. The N,N',N'', N'''-(9,9-dimethyl-9H-xanthene-2,4,5,7-tetrayl)urea derivs. I (R = substituent) were accessible from the

corresponding (9,9-dimethyl-9H-xanthene-2,4,5,6-tetrayl)carbamic acid tetra-Et ester. **Amino acid** derivs. II (R = H, alkyl, etc.; R1-R4 = substituent) were thus accessible from I.

ST **combinatorial library** tetraurea prepn; xanthenetetrayl urea prepn **combinatorial library; amino acid** xanthenetetrayl prepn **combinatorial library**

IT 55718-76-8, 2-Chloro-1,3,2-benzodioxaborole 171176-66-2, 9H-Xanthene-2,4,5,7-tetracarboxylic acid, 9,9-dimethyl-
RL: RCT (Reactant)
(soln.-phase generation of tetraurea **combinatorial libraries**)

IT 180037-91-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(soln.-phase generation of tetraurea **combinatorial libraries**)

IT 180037-92-7DP, derivs. 180037-93-8P 180037-94-9P 180037-95-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(soln.-phase generation of tetraurea **combinatorial libraries**)

L48 ANSWER 15 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:274584 HCAPLUS
DN 125:4694
TI Affinity-based **screening** of **combinatorial libraries** using automated serial-column chromatography
AU Evans, David M.; Williams, Kevin P.; McGuinness, Brian; Tarr, George; Regnier, Fred; Afeyan, Noubar; **Jindal, Satish**
CS PerSeptive Biosystems, Framingham, MA, 01701, USA
SO Nat. Biotechnol. (1996), 14(4), 504-507
CODEN: NABIF9; ISSN: 1087-0156
DT Journal
LA English
CC 9-3 (Biochemical Methods)
AB We have developed an automated serial chromatog. technique for **screening** a **library** of compds. based upon their relative affinity for a target mol. A "target" column contg. the immobilized target mol. is set in tandem with a reversed-phase column. A **combinatorial peptide library** is injected onto the target column. The target-bound **peptides** are eluted from the first column and transferred automatically to the reversed-phase column. The target-specific **peptide** peaks from the reversed-phase column are identified and sequenced. Using a monoclonal antibody (3E-7) against .beta.-endorphin as a target, we selected a single **peptide** with sequence YGGFL from approx. 5800 **peptides** present in a **combinatorial library**. We demonstrated the applicability of the technol. towards selection of **peptides** with predetd. affinity for bacterial lipopolysaccharide (LPS, endotoxin). We expect that this technol. will have broad applications for high throughput **screening** of **chem. libraries** or natural product exts.

ST **combinatorial library** chromatog

IT Chromatography
Combinatorial library
(affinity-based **screening** of **combinatorial libraries** using automated serial-column chromatog.)

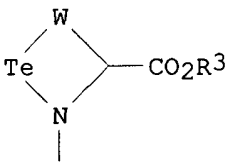
IT Lipopolysaccharides
Peptides, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(affinity-based **screening** of **combinatorial libraries** using automated serial-column chromatog.)

L48 ANSWER 16 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:969428 HCAPLUS
DN 124:8619
TI Preparation of xanthenecarboxamides as protease inhibitors
IN Rebek, Julius, Jr.; Carell, Thomas; **Wintner, Edward A.**

PA Massachusetts Institute of Technology, USA
SO PCT Int. Appl., 111 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D405-14
ICS A61K031-35; C07C061-125; A61K031-185; C07D311-82; A61K031-40
CC 27-14 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 34
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9519359	A1	19950720	WO 1995-US344	19950111
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9515628	A1	19950801	AU 1995-15628	19950111
US 5877030	A	19990302	US 1995-454861	19950531

PRAI US 1994-180215 19940112
US 1994-282083 19940728
WO 1995-US344 19950111
OS MARPAT 124:8619
GI

Q= 

AB **Combinatorial libraries** comprising J1J2XJ3J4 [J1,J3 = NH(CH2)aCHY(CH2)bCO2R1; J2 = NH(CH2)cCHZ(CH2)dCO2R2; J4 = N-attached heterocyclyl group Q; R1-R3 = H, alkyl, aryl, etc.; T, W = C (sic) or O; X = xanthene residue having groups J1-J4 covalently linked a positions 2,4,5, and 7, resp.; Y = hydrocarbyl; Z = hydrocarbyl group having a proton-accepting group; a-d = 0-2; e = 1-3] were prepd. as protease inhibitors (no data). Thus, 9,9-dimethylxanthene-2,4,5,7-tetracarboxylic acid tetrachloride (prepn. given) was amidated by 21 amino group-contg. compds. (e.g., **amino acids**) to give a **combinatorial library** theor. contg. 97,461 different **library** compds.
ST xanthenecarboxamide **combinatorial library** prepn protease inhibitor
IT **Combinatorial library**
(prepn. of xanthenecarboxamides as protease inhibitors)
IT 9002-07-7, Trypsin
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(inhibitors; prepn. of xanthenecarboxamides as protease inhibitors)
IT 9001-92-7, Proteinase
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(mediated diseases;treatment; prepn. of xanthenecarboxamides as protease inhibitors)
IT 165465-27-0DP, amides with **amino acids**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of xanthenecarboxamides as protease inhibitors)
IT 100-46-9, Benzylamine, reactions 107-10-8, Propylamine, reactions

108-91-8, Cyclohexylamine, reactions 2393-23-9, 4-Methoxybenzylamine 19814-75-6, 9,9-Dimethylxanthene 68858-20-8 98930-01-9 103213-32-7 109425-51-6 161980-55-8
RL: RCT (Reactant)
(prepn. of xanthenecarboxamides as protease inhibitors)

IT 165465-27-0P 166034-32-8P 171176-58-2P 171176-59-3P 171176-60-6P 171176-61-7P 171176-62-8P 171176-63-9P 171176-64-0P 171176-65-1P 171176-66-2P 171176-67-3P 171176-68-4P 171176-69-5P 171176-70-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of xanthenecarboxamides as protease inhibitors)

L48 ANSWER 17 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:924956 HCAPLUS
TI Efficient generation of tetraurea **libraries** on a rigid core.
AU **Shipps, G. W.**; Spitz, U. P.; Rebek, J. Jr.
CS Department Chemistry, Massachusetts Institute Technology, Cambridge, MA, 02139, USA
SO Book of Abstracts, 210th ACS National Meeting, Chicago, IL, August 20-24 (1995), Issue Pt. 2, ORGN-342 Publisher: American Chemical Society, Washington, D. C.
CODEN: 61XGAC
DT Conference; Meeting Abstract
LA English
AB Combinatorial approaches to the discovery of active mols. (inhibitors of **proteins**, drugs, **ligands**, etc.) depend heavily on two factors: the ability to synthesize a multitude of different mols. and to identify active compds. We have developed the methodol. to create ensembles of xanthene-based tetraureas with pendant **amino acid** Me ester groups (of the general form I). The synthetic and mechanistic details will be presented.

L48 ANSWER 18 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:802849 HCAPLUS
DN 123:221536
TI Selection of **peptides** with surface affinity for .alpha.-chymotrypsin using a phage display library
AU Krook, M.; Lindbladh, C.; **Birnbaum, S.**; Naess, H.; Eriksen, J. A.; Mosbach, K.
CS Department of Pure and Applied Biochemistry, Chemical Center, University of Lund, P.O. Box 124, Lund, S-221 00, Swed.
SO J. Chromatogr., A (1995), 711(1), 119-28
CODEN: JCRAEY
DT Journal
LA English
CC 7-3 (Enzymes)
Section cross-reference(s): 6
AB **Peptides** with affinity for the surface of .alpha.-chymotrypsin (EC 3.4.21.1) were selected from a hexapeptide phage display library consisting of 107 different clones. Seven selections were performed and five individual phage clones analyzed. Compared to the primary library, the five **peptide** phage clones all interacted more strongly with .alpha.-chymotrypsin, and **DNA** sequencing of the phage clones revealed five different **amino acid** sequences: Gly-Ala-Val-Ile-Thr-His, Arg-Asp-Ile-Val-Val-Ala, Val-Tyr-Ser-His-Ala-Ser, Gly-Ser-Tyr-Ser-Ala-Gly and Leu-Asp-Ile-Val-Val-Ala. Two of the **peptides** exhibited 83% identity (i.e. a difference of just one **amino acid**). The chem. synthesized **peptides** competitively reduced the binding of the corresponding **peptide** phage clone to .alpha.-chymotrypsin. Binding of some of the selected **peptide** phage clones to .alpha.-chymotrypsin was also reduced by several of the other non-corresponding synthesized **peptides**, suggesting that these **peptides** have common recognition areas on the enzyme. Three of the synthesized **peptides** were poor substrates of .alpha.-chymotrypsin and they did not inhibit enzyme activity. The results suggest that it is possible to select **peptides** from **peptide** phage display libraries with

affinity for different surface structures on the enzyme, not involved in the biol. active site.
ST chymotrypsin **peptide** binding phage display library
IT **Combinatorial library**
(selection of **peptides** with surface affinity for .alpha.-chymotrypsin using a phage display **library**)
IT Molecular structure-biological activity relationship
(chymotrypsin-binding, selection of **peptides** with surface affinity for .alpha.-chymotrypsin using a phage display library)
IT 9004-07-3, .alpha.-Chymotrypsin
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(selection of **peptides** with surface affinity for .alpha.-chymotrypsin using a phage display library)
IT 168331-06-4 168331-07-5 168331-08-6 168331-09-7 168331-10-0
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(selection of **peptides** with surface affinity for .alpha.-chymotrypsin using a phage display library)

L48 ANSWER 19 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:722871 HCAPLUS
DN 123:106912
TI A tandem-column chromatographic method for studying the interaction between **ligands** and their targets: lipopolysaccharide as a model
AU Evans, David M.; Williams, Kevin P.; Parsons, George; **Jindal, Satish**
CS PerSeptive Biosystems, Framingham, MA, 01701, USA
SO Anal. Biochem. (1995), 229(1), 42-7
CODEN: ANBCA2; ISSN: 0003-2697
DT Journal
LA English
CC 9-3 (Biochemical Methods)
Section cross-reference(s): 1, 10
AB The identification of a lead **ligand** from a **library** of compds. for a specific target requires both a selection process and a method to assess relative affinities. Using a tandem-column chromatog. technique, the authors developed a novel and rapid method for detn. of relative affinities for **ligands** binding to a specific target mol. They demonstrate, using known **ligands** for the lipid A region of lipopolysaccharide, that the relative affinities of these **ligands** can be detd. and may be used to characterize the competitive interaction between **ligands** for the same target. The method can be adapted toward **screening** of sol. **libraries** of **peptides** and small mols. and those **ligands** exhibiting a desired affinity can be rapidly selected for further characterization/development.
ST **ligand** interaction analysis tandem column chromatog; affinity **ligand** lipopolysaccharide detn; endotoxin **ligand** interaction analysis chromatog
IT Affinity
Chromatographs, column and liquid
Chromatography, column and liquid
Molecular association
(tandem-column chromatog. study of **ligand**-target interactions with lipopolysaccharide as model)
IT **Ligands**
Lipopolysaccharides
Peptides, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(tandem-column chromatog. study of **ligand**-target interactions with lipopolysaccharide as model)
IT Toxins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(endo-, tandem-column chromatog. study of **ligand**-target interactions with lipopolysaccharide as model)

affinity for different surface structures on the enzyme, not involved in the biol. active site.
ST chymotrypsin **peptide** binding phage display library
IT **Combinatorial library**
(selection of **peptides** with surface affinity for .alpha.-chymotrypsin using a phage display **library**)
IT Molecular structure-biological activity relationship
(chymotrypsin-binding, selection of **peptides** with surface affinity for .alpha.-chymotrypsin using a phage display library)
IT 9004-07-3, .alpha.-Chymotrypsin
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)
(selection of **peptides** with surface affinity for .alpha.-chymotrypsin using a phage display library)
IT 168331-06-4 168331-07-5 168331-08-6 168331-09-7 168331-10-0
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(selection of **peptides** with surface affinity for .alpha.-chymotrypsin using a phage display library)

L48 ANSWER 19 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:722871 HCAPLUS
DN 123:106912
TI A tandem-column chromatographic method for studying the interaction between **ligands** and their targets: lipopolysaccharide as a model
AU Evans, David M.; Williams, Kevin P.; Parsons, George; **Jindal, Satish**
CS PerSeptive Biosystems, Framingham, MA, 01701, USA
SO Anal. Biochem. (1995), 229(1), 42-7
CODEN: ANBCA2; ISSN: 0003-2697
DT Journal
LA English
CC 9-3 (Biochemical Methods)
Section cross-reference(s): 1, 10
AB The identification of a lead **ligand** from a **library** of compds. for a specific target requires both a selection process and a method to assess relative affinities. Using a tandem-column chromatog. technique, the authors developed a novel and rapid method for detn. of relative affinities for **ligands** binding to a specific target mol. They demonstrate, using known **ligands** for the lipid A region of lipopolysaccharide, that the relative affinities of these **ligands** can be detd. and may be used to characterize the competitive interaction between **ligands** for the same target. The method can be adapted toward **screening** of sol. **libraries** of **peptides** and small mols. and those **ligands** exhibiting a desired affinity can be rapidly selected for further characterization/development.
ST **ligand** interaction analysis tandem column chromatog; affinity **ligand** lipopolysaccharide detn; endotoxin **ligand** interaction analysis chromatog
IT Affinity
Chromatographs, column and liquid
Chromatography, column and liquid
Molecular association
(tandem-column chromatog. study of **ligand**-target interactions with lipopolysaccharide as model)
IT **Ligands**
Lipopolysaccharides
Peptides, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(tandem-column chromatog. study of **ligand**-target interactions with lipopolysaccharide as model)
IT Toxins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(endo-, tandem-column chromatog. study of **ligand**-target interactions with lipopolysaccharide as model)

L48 ANSWER 20 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:714118 HCAPLUS
DN 123:137853
TI Characterization of the Complexity of Small-Molecule Libraries by Electrospray Ionization Mass Spectrometry
AU Dunayevskiy, Yuriy; Vouros, Paul; Carell, Thomas; **Wintner, Edward A.**; Rebek, Julius, Jr.
CS Barnett Institute, Northeastern University, Boston, MA, 02115, USA
SO Anal. Chem. (1995), 67(17), 2906-15
CODEN: ANCHAM; ISSN: 0003-2700
DT Journal
LA English
CC 9-5 (Biochemical Methods)
Section cross-reference(s): 73, 80
AB The growing interest in **combinatorial chem.** has led the authors to explore new anal. methods for the anal. of complex mol. **libraries.** Because an investigation of large mixts. with 104-105 different **chem.** entities was not realistic, an alternative approach was pursued that included the anal. of small representative sublibraries using pos. and neg. ion electrospray mass spectrometry. The detailed anal. of these model mixts., contg. up to 55 components, allowed the authors to obtain important information about the compn. of a **library** with considerable complexity. The results were used to improve the synthetic procedure to provide the max. yield of expected **library** components. The applicability of mass spectrometry to the anal. of complex matrixes and the usefulness of the technique for **screening** synthesized **combinatorial libraries** to probe their expected diversity and complexity are demonstrated.
ST biomol **combinatorial library** electrospray mass spectrometry
IT **Combinatorial library**
(characterization of small-mol. **combinatorial libraries** by electrospray ionization mass spectrometry)
IT **Amino acids**, analysis
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(**peptides** contg.; characterization of small-mol. **combinatorial libraries** by electrospray ionization mass spectrometry)
IT Molecules
(biochem., characterization of small-mol. **combinatorial libraries** by electrospray ionization mass spectrometry)
IT Mass spectrometry
(electrospray-ionization, characterization of small-mol. **combinatorial libraries** by electrospray ionization mass spectrometry)
IT 56-40-6D, Glycine, **peptides** contg. 56-41-7D, Alanine, **peptides** contg. 56-45-1D, Serine, **peptides** contg. 56-84-8D, Aspartic acid, **peptides** contg. 56-85-9D, Glutamine, **peptides** contg. 56-86-0D, Glutamic acid, **peptides** contg. 56-87-1D, L-Lysine, **peptides** contg. 60-18-4D, Tyrosine, **peptides** contg. 61-90-5D, Leucine, **peptides** contg. 63-68-3D, Methionine, **peptides** contg. 63-91-2D, Phenylalanine, **peptides** contg. 70-47-3D, Asparagine, **peptides** contg. 71-00-1D, Histidine, **peptides** contg. 72-18-4D, Valine, **peptides** contg. 72-19-5D, Threonine, **peptides** contg. 73-22-3D, Tryptophan, **peptides** contg. 73-32-5D, Isoleucine, **peptides** contg. 74-79-3D, Arginine, **peptides** contg. 147-85-3D, Proline, **peptides** contg.
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(characterization of small-mol. **combinatorial libraries** by electrospray ionization mass spectrometry)

L48 ANSWER 21 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:599851 HCAPLUS
DN 123:102049
TI New promise in **combinatorial chemistry**: Synthesis,

characterization, and **screening** of small-molecule **libraries** in solution

AU Carell, Thomas; **Wintner, Edward A**; Sutherland, Andrew J; Rebek, Julius Jr; Dunayevskiy, Yuriy M; Vouros, Paul

CS Department Chemistry, Massachusetts Institute Technology, Cambridge, MA, 02139, USA

SO Chem. Biol. (1995), 2(3), 171-83
CODEN: CBOLE2; ISSN: 1074-5521

DT Journal

LA English

CC 1-4 (Pharmacology)

AB The increasing interest in **combinatorial chem.** as a tool for the development of therapeutics has led to many new methods of creating mol. **libraries** of potential lead compds. Current methods have made it possible to develop **libraries** of several million compds. As a result, the limiting factor in the **screening** of **libraries** has become the identification and characterization of active species. The authors have recently described a method for generating **libraries** of water-sol. compds. contg. mixts. of 104 to 105 different small org. mols. by using generally applicable soln. phase **chem.** The authors set out to develop new methods to characterize and decode these **libraries. Libraries** were generated by condensing a multi-acid-chloride core mol. with various amines, producing mols. with functional groups about a rigid backbone. Compn. and complexity of the **libraries** was evaluated using electrospray mass spectrometry to analyze model **libraries** contg. .ltoreq.55 different mols. The no. of peaks obtained in mass spectrometry is directly correlated with the complexity of the **library**, and the authors were therefore able to deduce which of the expected compds. had in fact been formed in the **library**, and which of the building blocks in the **library** were not efficiently used. An iterative selection procedure was developed using this information, which allowed the **screening** of **libraries** of .ltoreq.50,000 **chem.** species to produce a competitive inhibitor of the enzyme trypsin. The authors' strategy for the identification of active species should be broadly applicable to other methods of generating complex **libraries** of small mols. The selection from the **library** of a compd. with desired biol. properties augurs well for the potential value of generating and **screening** complex mixts. of small mols. in soln.

ST **combinatorial library chem** pharmacol **screening**; trypsin inhibitor **combinatorial library** acid chloride

IT **Combinatorial library**
Pharmacology
(new promise in **combinatorial chem.** in relation to synthesis and characterization and pharmacol. **screening** of small-mol. **libraries** in soln. as trypsin inhibitors)

IT 9002-07-7, Trypsin
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(inhibitors; new promise in **combinatorial chem.** in relation to synthesis and characterization and pharmacol. **screening** of small-mol. **libraries** in soln. as trypsin inhibitors)

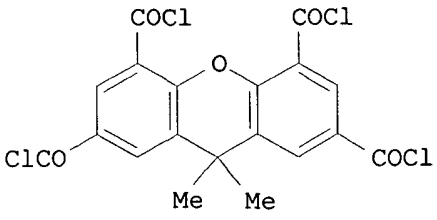
IT 77354-22-4D, 1,3,5-Benzenetriacetyl trichloride, derivs. 161980-55-8D, derivs. 165465-27-0D, derivs. 166034-31-7D, derivs. 166034-32-8D, derivs.
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); BIOL (Biological study)
(new promise in **combinatorial chem.** in relation to synthesis and characterization and pharmacol. **screening** of small-mol. **libraries** in soln. as trypsin inhibitors)

IT 166034-37-3P 166034-38-4P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(new promise in **combinatorial chem.** in relation to

synthesis and characterization and pharmacol. **screening** of small-mol. **libraries** in soln. as trypsin inhibitors)

IT 166034-33-9P 166034-34-0P 166034-35-1P 166034-36-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(new promise in **combinatorial chem.** in relation to synthesis and characterization and pharmacol. **screening** of small-mol. **libraries** in soln. as trypsin inhibitors)

L48 ANSWER 22 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:542626 HCAPLUS
DN 123:74100
TI **Screening** method for isolation in solution of biologically active compounds from a molecular library
AU Carell, Thomas; **Wintner, Edward A.**; Rebek, Julius Jr.
CS Dep. Chem., Massachusetts Inst. Technol., Cambridge, MA, 02139, USA
SO Angew. Chem. (1994), 106(20), 2162-4 (See also Angew. Chem., Int. Ed. Engl., 1994, 33(20), 2061-4)
CODEN: ANCEAD; ISSN: 0044-8249
DT Journal
LA German
CC 1-1 (Pharmacology)
Section cross-reference(s): 21
GI



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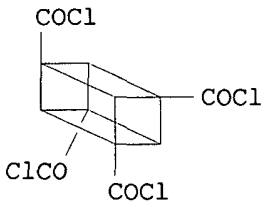

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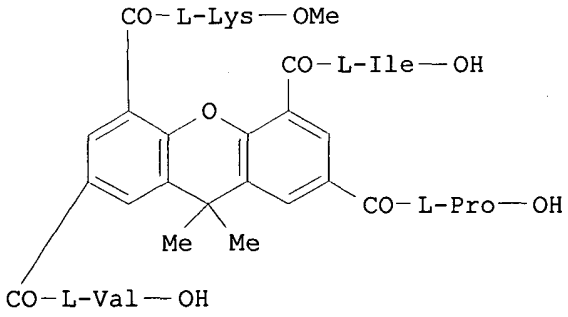


III

AB I and II were condensed with 19 **amino acids** to produce a **combinatorial library**. A method is described whereby this **library** was **screened** for trypsin-inhibitory activity. The most active compd. in this assay was III.

ST **combinatorial library** trypsin inhibitor xanthene **peptide**; cubane **peptide** trypsin inhibitor **combinatorial library**; **peptide** cubane xanthene antitrypsin **combinatorial library**

IT **Amino acids**, biological studies
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reaction products with xanthenetetracarboxylic acid chloride or cubanetetracarboxylic acid chloride; **screening** method for

isolation in soln. of biol. active compds. from a mol. library)
IT **Combinatorial library**
(**screening** method for isolation in soln. of biol. active compds. from a mol. **library**)
IT 9002-07-7, Trypsin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; **screening** method for isolation in soln. of biol. active compds. from a mol. library)
IT 161980-55-8 165465-27-0 165465-28-1 165465-29-2
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reaction products with **amino acids**; **screening** method for isolation in soln. of biol. active compds. from a mol. library)

L48 ANSWER 23 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:542625 HCAPLUS
DN 123:142992
TI Novel method for preparation of **libraries** of small organic molecules
AU Carell, Thomas; **Wintner, Edward A.**; Bashir-Hashemi, A.; Rebek, Julius, Jr.
CS Dep. Chem., Massachusetts Inst. Technol., Cambridge, MA, 02139, USA
SO Angew. Chem. (1994), 106(20), 2159-62 (See also Angew. Chem., Int. Ed. Engl., 1994, 33(20), 2059-61)
CODEN: ANCEAD; ISSN: 0044-8249
DT Journal
LA German
CC 21-3 (General Organic Chemistry)
AB Amidation of 9,9-dimethyl-9H-xanthene-2,4,5,7-tetracarbonyl tetrachloride with amines. L-**amino acids** and heterocyclic compds. gave a series of products which represent a **library** of small org. mols. Similarly, cubanetetracarbonyl tetrachloride was also used to prep. product mixts. The product mixts. were analyzed by chromatog. and sepd. by HPLC and analyzed by mass spectroscopy.
ST *small org mol* **library** *prepn; xanthenetetracarboxamide small org mol* **library**; cubanetetracarboxamide small org mol **library**
IT Amines, reactions
Amino acids, reactions
Heterocyclic compounds
RL: RCT (Reactant)
(novel method for prepn. of **libraries** of small org. mols.)
IT 19814-75-6, 9H-Xanthene, 9,9-dimethyl 161980-60-5, Pentacyclo[4.2.0.02,5.03,8.04,7]octane-1,2,3,7-tetracarbonyl tetrachloride
RL: RCT (Reactant)
(novel method for prepn. of **libraries** of small org. mols.)
IT 165465-27-0P, 9H-Xanthene-2,4,5,7-tetracarbonyl tetrachloride, 9,9-dimethyl
RL: SPN (Synthetic preparation); PREP (Preparation)
(novel method for prepn. of **libraries** of small org. mols.)

L48 ANSWER 24 OF 24 HCAPLUS COPYRIGHT 2001 ACS
AN 1990:472238 HCAPLUS
DN 113:72238
TI Cloning and characterization of the yeast chaperonin HSP60 gene
AU Johnson, Rollin B.; Fearon, Kathleen; Mason, Thomas; **Jindal, Satish**
CS Whitehead Inst. Biomed. Res., Cambridge, MA, 02142, USA
SO Gene (1989), 84(2), 295-302
CODEN: GENED6; ISSN: 0378-1119
DT Journal
LA English
CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 6
AB The heat-shock **protein**, HSP60, is abundant in prokaryotes and

eukaryotes and is required in the assembly of specific **proteins**. The Saccharomyces cerevisiae HSP60 gene was cloned from a .lambda.gt11 genomic **library** using monoclonal antibodies. Its sequence and transcription start point were detd. It exists as a single copy. The predicted HSP60 contains a mitochondrial target sequence and exhibits striking **amino acid** sequence similarity to its counterparts in bacteria, plants, and humans. These data indicate a high level of evolutionary conservation and are consistent with the suggestion of evolutionarily conserved function (S.M. Hemmingsen et al., 1988).

ST Saccharomyces gene chaperonin HSP60 cloning sequence

IT Saccharomyces cerevisiae
(*chaperonin HSP60 gene of, cloning and sequence of*)

IT Molecular cloning
(of chaperonin HSP60 gene, of Saccharomyces cerevisiae)

IT **Protein** sequences
(of gene HSP60 chaperonin, of Saccharomyces cerevisiae, complete)

IT Deoxyribonucleic acid sequences
(chaperonin 60-specifying, of Saccharomyces cerevisiae, complete)

IT **Proteins**, specific or class
RL: BIOL (Biological study)
(chaperonins 60, gene for, of yeast, nucleotide and encoded **peptide** sequences of)

IT Gene and Genetic element, microbial
(promoter, of gene HSP60, of yeast, characterization of)

IT Gene and Genetic element, microbial
RL: BIOL (Biological study)
(HSP60, for chaperonin, of yeast, nucleotide and encoded **peptide** sequences of)

IT 123897-98-3, **Protein** hsp 60 (Saccharomyces cerevisiae reduced)
RL: PRP (Properties)
(**amino acid** sequence of)

IT 128634-96-8, Deoxyribonucleic acid (Saccharomyces cerevisiae clone Y3098/Y3099 gene HSP60)
RL: PRP (Properties); BIOL (Biological study)
(nucleotide sequence of)

=> d 165 bib abs tot

L65 ANSWER 1 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 2001:333650 HCAPLUS
DN 134:337938
TI Computer system and process for identifying a charge distribution which minimizes electrostatic contribution to binding at binding between a **ligand** and a molecule in a solvent and uses thereof
IN Tidor, Bruce; Lee, Lee-Peng; Dempster, Sara E.
PA Massachusetts Institute of Technology, USA
SO U.S., 24 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6230102	B1	20010508	US 1998-55475	19980403 <--
PRAI US 1997-42692	P	19970404 <--		

AB The present computer-implemented process involves a methodol. for detg. properties of **ligands** which in turn can be used for designing **ligands** for binding with **protein** or other mol. targets, for example, HIV targets. The methodol. defines the electrostatic complement for a given target site and geometry. The electrostatic complement may be used with steric complement for the target site to discover **ligands** through explicit construction and through the design or bias of **combinatorial libraries**. The definition of an electrostatic complement, i.e., the optimal tradeoff between unfavorable desolvation energy and favorable interactions in the

complex, has been discovered to be useful in **ligand** design. This methodol. essentially inverts the design problem by defining the properties of the optimal **ligand** based on phys. principles. These properties provide a clear and precise std. to which trial **ligands** may be compared and can be used as a template in the modification of existing **ligands** and the de novo construction of new **ligands**. The electrostatic complement for a given target site is defined by a charge distribution which minimizes the electrostatic contribution to binding at the binding sites on the mol. in a given solvent. One way to represent the charge distribution in a computer system is as a set of multipoles. By identifying mols. having point charges that match this optimum charge distribution, the detd. charge distribution may be used to identify **ligands**, to design drugs, and to design **combinatorial libraries**.

RE.CNT 27
RE
(3) Bharadwaj; Journal of Computational Chemistry 1995, V16(7), P898 HCAPLUS
(5) Caflisch; J Med Chem 1993, V36, P2142 HCAPLUS
(6) Connolly; J Appl Cryst 1983, V16, P548 HCAPLUS
(8) Eisen; PROTEINS: Structure, Function, and Genetics 1994, V19, P199 HCAPLUS
(9) Friedman; Biophysical Journal 1995, V69, P1528 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 2 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 2001:91445 HCAPLUS
DN 134:158472
TI Synthetic transcriptional modulator **ligands** and their use in gene regulation with chimeric **proteins** containing DNA-binding domains and **ligand**-binding domains
IN Verdine, Gregory L.; Nyanguile, Origene
PA President and Fellows of Harvard College, USA
SO U.S., 38 pp., Cont.-in-part of U.S. Ser. No. 987,912.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6183965	B1	20010206	US 1998-208057	19981209 <--
	US 6153383	A	20001128	US 1997-987912	19971209 <--
PRAI	US 1997-987912	A2	19971209 <--		

AB Novel synthetic transcriptional modulators having at least one selected **ligand** linked to at least one transcriptional modulating portion are described. The transcriptional modulators of the present invention can include a **ligand** linked to a **chem**. moiety. These transcriptional modulators can be used to selectively control gene expression and to identify components of the transcriptional machinery. Thus, the covalent conjugate (designated L-1) of FK506 and a 29-**amino acid peptide** of herpes simplex virus VP16 activator domain stimulates transcription in the presence of the chimeric GAL4-FKBP **protein**, but was unable to stimulate in the absence of GAL4-FKBP and the activation potential was significantly reduced in the presence of added rapamycin or GST-FKBP. Since acyclic **peptides** having the natural L stereochem. configuration are highly susceptible to proteolysis, the analogous conjugate (D-1) bearing nonnatural D stereochem. is prepd. D-1 reproducibly stimulated transcription to a significant extent, though to a slightly lesser extent than L-1. The synthesis of a **combinatorial** compd. **library** is also provided, and various **library** components are active transcriptional modulators when coupled to the HATU analog of FK506.

RE.CNT 30
RE
(1) Anon; WO 9101379 1991 HCAPLUS
(2) Anon; WO 9418317 1994 HCAPLUS
(3) Anon; WO 9502684 1995 HCAPLUS

(4) Anon; WO 9606110 1996 HCAPLUS
(5) Anon; WO 9606111 1996 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 3 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:511313 HCAPLUS
DN 131:139483
TI Discovery, development, and use of **protein** folding inhibitors
IN Netzer, William J.
PA USA
SO PCT Int. Appl., 116 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9940435	A1	19990812	WO 1999-US2612	19990206 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9925900	A1	19990823	AU 1999-25900	19990206 <--
PRAI	US 1998-74070	P	19980209 <--		
	WO 1999-US2612	W	19990206		

AB The subject disclosure relates to strategies and methods for the discovery, development, and use of drugs and drug lead mols. that inhibit **protein** folding (folding inhibitors). These can consist of small org. mols. that bind nascent **polypeptides** selectively within cells during their synthesis on ribosomes and/or before folding of the **protein** is completed, and by virtue of this activity inhibit the target **polypeptide** from folding to its native state which is otherwise responsible for its biol. activities. Methods for discovering folding inhibitors include e.g. (1) the design of specific **peptide** and nonpeptide inhibitors, (2) the identification of suitable **chemistries** for the synthesis of **combinatorial libraries** of small org. mols., (3) aptamers, and (4) effective screening methods. The present invention also relates to methods of enhancing the potencies of said compds., which are expected to have extraordinary medicinal properties.
RE.CNT 2
RE
(1) Bowie; US 5585277 A 1996 HCAPLUS
(2) Bowie; US 5679582 A 1997 HCAPLUS

L65 ANSWER 4 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:405112 HCAPLUS
DN 131:56155
TI Methods for the simultaneous identification of novel biological targets and lead structures for drug development using **combinatorial libraries** and probes
IN Heefner, Donald L.; Zepp, Charles M.; Gao, Yun; Jones, Steven W.
PA Sepracor Inc., USA
SO PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9931267	A1	19990624	WO 1998-US26894	19981218 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,				

DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9919256 A1 19990705 AU 1999-19256 19981218 <--
EP 1049796 A1 20001108 EP 1998-964053 19981218 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
PRAI US 1997-68035 P 19971218 <--
WO 1998-US26894 W 19981218

AB The **combinatorial** screening assays and detection methods of the present invention encompass highly diversified **libraries** of compds. which act as fingerprints to allow for the identification of specific mol. differences existing between biol. samples. The **combinatorial** screening assay and detection methods of the present invention utilize highly diversified **libraries** of compds. to interrogate and characterize complex mixts. in order to identify specific mol. differences existing between biol. samples, which may serve as targets for diagnosis of development of therapeutics. The invention is base, in part, on the design of sensitive, rapid, homogeneous assay systems that permit the evaluation, interrogation, and characterization of samples using complex, highly diversified **libraries** of mol. probes. The ability to run the high throughput assays in a homogeneous format increases sensitivity of screening. In addn., the homogeneous format allows the mols. which interact to maintain their native or active conformations. Moreover, the homogeneous assay systems of the invention utilize robust detection systems that do not require sepn. steps for detection of reaction products. The assays of the invention can be used for diagnostics, drug screening and discovery, target-driven discover, and in the field of proteomics and genomics for the identification of disease markers and drug targets.

RE.CNT 1
RE
(1) Lin; Science 1997, V278, P840 HCAPLUS

L65 ANSWER 5 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:390464 HCAPLUS
DN 131:39762
TI Method to identify transcriptional modulators
IN Verdine, Gregory L.; Nyanguile, Origene
PA President and Fellows of Harvard College, USA
SO PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9930164	A1	19990617	WO 1998-US26101	19981209 <--
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6153383	A	20001128	US 1997-987912	19971209 <--
AU 9919059	A1	19990628	AU 1999-19059	19981209 <--
EP 1038183	A1	20000927	EP 1998-963814	19981209 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI US 1997-987912 A 19971209 <--
WO 1998-US26101 W 19981209

AB Novel synthetic transcriptional modulators having at least one selected **ligand** linked to at least one transcriptional modulating portion are described. The transcriptional modulators of the present invention can include a **ligand** linked to a chem. moiety. These

transcriptional modulators can be used to selectively control gene expression and to identify components of the transcriptional machinery.

RE.CNT 3

RE

(1) Ariad Gene Therapeutics Incorporated; WO 9641865 A 1996 HCAPLUS

(2) Bujard, H; WO 9601313 A 1996 HCAPLUS

(3) Oncogene Science; WO 9101379 A 1991 HCAPLUS

L65 ANSWER 6 OF 49 HCAPLUS COPYRIGHT 2001 ACS

AN 1999:388066 HCAPLUS

DN 131:39708

TI Anti-picornaviral **ligands** via a **combinatorial** computational and synthetic approach

IN Joseph-McCarthy, Diane M.; Isaacs, Lyle D.; Whitesides, George M.; Karplus, Martin; Hogle, James M.; Cheh, James Li-wen

PA The President & Fellows of Harvard College, USA

SO PCT Int. Appl., 44 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9929280	A2	19990617	WO 1998-US26352	19981211 <--
	WO 9929280	A3	19990812		

W: AU, CA, JP, US

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRAI US 1997-69300 19971211 <--

AB The present invention provides structure-based **combinatorial libraries** of compds. contg. the functional group min. of picornaviruses including poliovirus and rhinovirus. The **libraries** can be used to screen for therapeutical antiviral compds., e.g., anti-picornaviral capsid-binding compds.

L65 ANSWER 7 OF 49 HCAPLUS COPYRIGHT 2001 ACS

AN 1999:375416 HCAPLUS

DN 131:27965

TI Prevention and treatment of amyloidogenic disease, especially Alzheimer's disease, based on induction of anti-amyloid immune response

IN Schenk, Dale B.

PA Athena Neurosciences, Inc., USA

SO PCT Int. Appl., 113 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9927944	A1	19990610	WO 1998-US25386	19981130 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9917061	A1	19990616	AU 1999-17061	19981130 <--
	EP 1033996	A1	20000913	EP 1998-961833	19981130 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	BR 9815357	A	20001024	BR 1998-15357	19981130 <--
	NO 2000002784	A	20000731	NO 2000-2784	20000531 <--
PRAI	US 1997-67740	P	19971202 <--		
	US 1998-80970	P	19980407		

WO 1998-US25386 W 19981130
AB The invention provides compns. and methods for treatment of amyloidogenic diseases. The methods entail administering an agent that induces a beneficial immune response against an amyloid deposit in the patient. The methods are particularly useful for prophylactic and therapeutic treatment of Alzheimer's disease. In such methods, a suitable agent is A.beta. peptide or an antibody thereto.
RE.CNT 2
RE
(1) McMichael; EP 0526511 B1 1997 HCAPLUS
(2) Prieels; WO 940015306 PCT Int Appl 1994 HCAPLUS

L65 ANSWER 8 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:273628 HCAPLUS
DN 130:278961
TI Method for identifying optimal binding **ligands** to a receptor.
IN Huse, William D.; Freedman, Michael H.
PA Ixsys, Inc., USA
SO PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9919506	A2	19990422	WO 1998-US21390	19981008 <--
	WO 9919506	A3	19990729		
	W: AU, CA, JP, NZ				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9897966	A1	19990503	AU 1998-97966	19981008 <--
	EP 1025256	A2	20000809	EP 1998-952213	19981008 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	US 1997-112011	P	19971009 <--		
	US 1997-948187	A	19971009 <--		
	WO 1998-US21390	W	19981008		

AB The present invention provides a method for detg. binding of a receptor to one or more **ligands**. The method consists of contacting a collective receptor variant population with one or more **ligands** and detecting binding of one or more **ligands** to the collective receptor variant population. The collective receptor variant population can be further divided into two or more subpopulations, one or more of the two or more subpopulations can be contacted with one or more **ligands** and one or more receptor variant subpopulations having binding activity to one or more **ligands** can be detected. The steps of dividing, contacting and detecting can be repeated one or more times. The invention also provides methods for identifying a receptor variant having optimal binding activity to one or more **ligands**. The invention addnl. provides a method for detg. binding of a **ligand** to one or more receptors. The method consists of contacting a collective **ligand** variant population with one or more receptors and detecting binding of one or more receptors to the collective **ligand** variant population. As with the variant receptor population, the methods for detg. binding of a **ligand** to one or more receptors can include the steps of further dividing, contacting and detecting one or more **ligand** variants having binding activity to one or more receptors. The invention also provides methods for identifying a **ligand** or **ligand** variant having optimal binding activity.

L65 ANSWER 9 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:81633 HCAPLUS
DN 130:105305
TI Prosaposin receptor assay for identification of prosaposin receptor agonists and antagonists

IN Parks, D. Elliot
PA Myelos Neurosciences Corporation, USA
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9904262	A1	19990128	WO 1998-US14296	19980709 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9884807	A1	19990210	AU 1998-84807	19980709 <--
	EP 996856	A1	20000503	EP 1998-935595	19980709 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	US 1997-896181		19970717 <--		
	WO 1998-US14296		19980709		

AB Methods of identifying prosaposin receptor agonists and antagonists. Chem. **libraries** are screened with the purified receptor on transfected cells expressing the prosaposin receptor to det. which compds. bind to the receptor. Compds. which bind to the receptor are then tested using functional assays to identify receptor agonists and antagonists.
RE.CNT 2
RE
(1) O'Brien, J; WO 9503821 A 1995 HCAPLUS
(2) The Regents Of The University Of California; WO 9839357 A 1998 HCAPLUS

L65 ANSWER 10 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:34408 HCAPLUS
DN 130:90492
TI Lawn assay for compounds that affect enzyme activity or bind to target molecules
IN Chelsky, Daniel; Burbaum, Jonathan J.
PA Pharmacopeia, Inc., USA
SO U.S., 16 pp., Cont.-in-part of U.S. Ser. No. 436,120, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5856083	A	19990105	US 1995-553056	19951103 <--
	US 5688997	A	19971118	US 1995-482488	19950607 <--
	WO 9716569	A1	19970509	WO 1996-US17702	19961024 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI				
	AU 9675535	A1	19970522	AU 1996-75535	19961024 <--
PRAI	US 1994-239302		19940506 <--		
	US 1995-436120		19950508 <--		
	US 1995-553056		19951103 <--		
	WO 1996-US17702		19961024 <--		

AB A lawn assay is described for detg. compds. that affect enzyme activity or that bind to target mols. Compds. to be screened are cleaved, and diffused from solid supports into a colloidal matrix. Enzymic catalysis

or binding to target mols. by the compds. is carried out in the matrix. Active compds. are found by monitoring a photometrically detectable change in a substrate, coenzyme, or cofactor involved in the enzymic reaction, or in a labeled **ligand** bound to the target mol., that produces a zone of activity assocd. with the compds. The methodol. of the invention is useful for drug screening.

RE.CNT 18
RE
(1) Anon; WO 9200091 1992 HCAPLUS
(2) Anon; WO 9200091 1992 HCAPLUS
(3) Anon; WO 9402515 1994 HCAPLUS
(4) Anon; WO 9402515 1994 HCAPLUS
(5) Anon; WO 9408051 1994 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 11 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:19918 HCAPLUS
DN 130:204594
TI The generation of carbohydrate-based **combinatorial libraries** for drug discovery
AU Sofia, Michael J.
CS Intercardia Research Laboratories, Intercardia, Inc., Cranbury, NJ, 08512, USA
SO Med. Chem. Res. (**1998**), 8(7/8), 362-378
CODEN: MCREEB; ISSN: 1054-2523
PB Birkhaeuser Boston
DT Journal; General Review
LA English
AB A review with 24 refs. The authors discuss how carbohydrate scaffolds are biol. relevant mol. platforms that can be used to identify unique **ligands** for a wide variety of biomol. drug targets. The authors have developed solid phase **combinatorial chem.** strategies using monosaccharide and disaccharide scaffolds for pharmacophore mapping of small-mol. **protein** interactions and **protein-protein** interactions. They are exploiting these strategies for identifying novel antibacterial agents, but expect that these **libraries** will find broad relevance as mol. screening tests.

RE.CNT 24
RE
(3) Boojamra, C; J Org Chem 1997, V62, P1240 HCAPLUS
(4) DeNinno, M; J Med Chem 1997, V40, P2547 HCAPLUS
(5) Dewitt, S; Proc Natl Acad Sci USA 1993, V90, P6909 HCAPLUS
(6) Evans, B; J Med Chem 1988, V31, P2235 HCAPLUS
(7) Gallop, M; J Med Chem 1994, V37, P1233 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 12 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:8206 HCAPLUS
DN 130:63329
TI **Combinatorial** process for preparing substituted phenylalanine **libraries** for use in assay kits and automated assay machines
IN Heerding, Julia Marie; Lampe, John William
PA Eli Lilly and Company, USA
SO PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI WO 9857173	A1	19981217	WO 1998-US11909	19980610	<--

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,

UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
AU 9880630 A1 19981230 AU 1998-80630 19980610 <--
PRAI US 1997-49054 19970610 <--
WO 1998-US11909 19980610
OS MARPAT 130:63329
AB This invention relates to a novel diverse **combinatorial library** of substituted phenylalanine compds. and to an app. providing a readily accessible source of individual members of the **library**. The app. can be used in assay kits and as a replaceable element in automated assay machines. Merrifield resin was reacted with p-nitrophenyl-N-Boc-phenylalanine, the amino-protecting group was removed, and the resin-bound product was acylated. The nitro group was reduced and a second acylation was performed.
RE.CNT 7
RE
(1) Chugi Seiyaku Kabushiki Kaisha; WO 9618607 A1 1996 HCAPLUS
(2) Degraw, J; J Med Chem 1972, V15(7), P781 HCAPLUS
(3) Gordon; J Med Chem 1994, V37(10), P1385 HCAPLUS
(4) Ouihia, A; Tetrahedron Letters 1992, V33(38), P5509 HCAPLUS
(5) Pfizer Limited; EP 0358398 A1 1990 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 13 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:710330 HCAPLUS
DN 130:119528
TI Encoded chemical synthesis coupled to screening: "Pot Assay"
AU Parandoosh, Z.; Knowles, S. K.; Xiao, X-Y.; Zhao, C.; David, G. S.; Nova, M. P.
CS IRORI, La Jolla, CA, 92037-1031, USA
SO Comb. Chem. High Throughput Screening (**1998**), 1(3), 135-142
CODEN: CCHSFU; ISSN: 1386-2073
PB Bentham Science Publishers
DT Journal
LA English
AB A variety of screening methodologies is available to identify lead compds. Screening methods that would permit the direct use of **libraries** made via the Radiofrequency Encoded **Combinatorial chem**. paradigm (each individual small mol. in the **library** is presented sep. on an individual encoded support) have the potential to diminish burdensome steps in this process. Here we report on our studies leading to such a direct method, which we have termed a Pot Assay. Pot Assay is a multiplex assay, which simultaneously measures specific binding of a no. of **ligands** to at least one target. Pot Assay uses specific radiofrequency signals to decode compds. that are high affinity binders. We validated this approach by evaluating the interaction of biotin and its analogs with labeled streptavidin. This report introduces Pot Assay as a rapid, simple, sensitive and accurate format for identifying active members of **libraries** synthesized on solid supports. The success of this study demonstrates the power of coupling Radiofrequency Encoded **Combinatorial chem**. and screening. This assay format may be applied to a wide range of screens that are based on binding events: **ligand**/receptor, inhibitor/enzyme, antigen/antibody, **protein/protein**, DNA/**protein**, and RNA/DNA.
RE.CNT 29
RE
(3) Brown, A; Anal Biochem 1994, V217, P139 HCAPLUS
(4) Chen, J; J Am Chem Soc 1993, V115, P12591 HCAPLUS
(5) Cook, N; DDT 1996, V1, P287 HCAPLUS
(6) David, G; Bichem Biophys Res Commun 1972, V48, P464 HCAPLUS
(7) Devlin, J; Science 1990, V249, P404 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 14 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:710328 HCAPLUS
DN 130:118884
TI **Combinatorial libraries**: studies in molecular recognition
AU Nestler, H. Peter; Liu, Ruiping
CS Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, 11724, USA
SO Comb. Chem. High Throughput Screening (**1998**), 1(3), 113-126
CODEN: CCHSFU; ISSN: 1386-2073
PB Bentham Science Publishers
DT Journal; General Review
LA English
AB A review with 129 refs. In recent years, **combinatorial libraries** have become a major tool for drug discovery and drug development. Along the way, one potential use of **combinatorial chem. libraries** almost been neglected: the basic study of intermol. interactions. Esp. "one-bead-one-structure" **libraries** can be a powerful means for the discovery of **ligands** to synthetic receptors and vice versa. Encoded **combinatorial libraries** have been used to disclose **ligands** for well designed macrocyclic host mols. and to elucidate their specificities for **peptide** sequences. These studies led via receptors with more flexibility to simple host mols. without elaborate design that are accessible to **combinatorial** synthesis. These findings open a realm of possibilities and applications. An intriguing one is the development of **chem.** sensors for analytes that are otherwise hard or only unspecifically detected. Furthermore, such **libraries** and the techniques that were developed to handle them have been used to find new catalysts and enzyme mimics. In this review we put the emphasis on studies involving "one-bead-one-structure" **libraries**. We will review the techniques to generate them, to encode and analyze them, and to assay them. We will describe their past usage and the intriguing results of these studies and point out interesting new applications of such **libraries** for the study of non-covalent intermol. interactions.
RE.CNT 129
RE
(2) Balkenhohl, F; Angew Chem Int Ed Engl 1996, V35, P2288 HCAPLUS
(3) Berg, T; Bioorg Med Chem Lett 1998, V8, P1221 HCAPLUS
(4) Berk, S; Bioorg Med Chem Lett 1997, V7, P837 HCAPLUS
(5) Bonnat, M; Tetrahedron Lett 1996, V37, P5409 HCAPLUS
(6) Borchardt, A; J Am Chem Soc 1994, V116, P373 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L65 ANSWER 15 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:557328 HCAPLUS
DN 129:269868
TI Phage-displayed **peptide libraries**
AU Zwick, Michael B.; Shen, Juqun; Scott, Jamie K.
CS Institute of Molecular Biology and Biochemistry, Biochemistry Program and the Department of Biological Sciences, Simon Fraser University, Burnaby, BC, V5A 1S6, Can.
SO Curr. Opin. Biotechnol. (**1998**), 9(4), 427-436
CODEN: CUOBE3; ISSN: 0958-1669
PB Current Biology Ltd.
DT Journal; General Review
LA English
AB A review with 72 refs. Over the past year, significant advances have been achieved through the use of phage-displayed **peptide libraries**. A wide variety of bioactive mols., including antibodies, receptors and enzymes, have selected high-affinity and/or highly-specific **peptide ligands** from a no. of different types of **peptide library**. The demonstrated therapeutic potential of some of these **peptides**, as well as new insights into **protein** structure and function that **peptide ligands** have provided, highlight the progress

made within this rapidly-expanding field.

L65 ANSWER 16 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:543225 HCAPLUS
DN 129:146647
TI **Protein** fragment complementation assays to detect biomolecular interactions
IN Michnick, Stephen William Watson; Pelletier, Joelle Nina; Remy, Ingrid
PA Universite De Montreal, Can.
SO PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9834120	A1	19980806	WO 1998-CA68	19980202 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2196496	AA	19980731	CA 1997-2196496	19970131 <--
AU 9858505	A1	19980825	AU 1998-58505	19980202 <--
EP 966685	A1	19991229	EP 1998-901905	19980202 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI CA 1997-2196496 19970131 <--
WO 1998-CA68 19980202 <--

AB We describe a strategy for designing and implementing **protein** -fragment complementation assays (PCAs) to detect biomol. interactions in vivo and in vitro. The design, implementation and broad applications of this strategy are illustrated with a large no. of enzymes with particular detail provided for the example of murine dihydrofolate reductase (DHFR). Fusion **peptides** consisting of N- and C-terminal fragments of murine DHFR fused to GCN4 leucine zipper sequences were coexpressed in Escherichia coli grown in minimal medium, where the endogenous DHFR activity was inhibited with trimethoprim. Coexpression of the complementary fusion products restored colony formation. Survival only occurred when both DHFR fragments were present and contained leucine-zipper forming sequences, demonstrating that reconstitution of enzyme activity requires assistance of leucine zipper formation. DHFR fragment-interface point mutants of increasing severity (Ile to Val, Ala and Gly) resulted in a sequential increase in E. coli doubling times illustrating the successful DHFR fragment reassembly rather than non-specific interactions between fragments. This assay could be used to study equil. and kinetic aspects of mol. interactions including **protein-protein**, **protein**-DNA, **protein** -RNA, **protein**-carbohydrate and **protein**-small mol. interactions, for screening cDNA **libraries** for binding of a target **protein** with unknown **proteins** or **libraries** of small org. mols. for biol. activity. The selection and design criteria applied here is developed for numerous examples of clonal selection, colorimetric, fluorometric and other assays based on enzymes whose products can be measured. The development of such assay systems is shown to be simple, and provides for a diverse set of **protein** fragment complementation applications.

L65 ANSWER 17 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:518718 HCAPLUS
DN 129:239362
TI **Combinatorial** and computational approaches in structure-based drug design

AU Kubinyi, Hugo
CS Combinatorial Chemistry and Molecular Modelling, ZHF/G-A30, BASF AG, Ludwigshafen, D-67056, Germany
SO Curr. Opin. Drug Discovery Dev. (**1998**), 1(1), 16-27
CODEN: CODDFF; ISSN: 1367-6733
PB Current Drugs Ltd.
DT Journal; General Review
LA English
AB A review, with 112 refs. The increasing no. of **protein** 3D structures and the success of structure-based approaches has led to the development of several exptl. and theor. techniques for the rational design of **protein ligands**. **Combinatorial chem.** significantly speeds up the synthesis of potential new drug candidates. Diversity considerations, as well as the use of 3D structural information of the biol. targets, reduce the size of huge **libraries** to a reasonable no. of rationally-designed **ligands**. New NMR techniques (SAR by NMR) allow the construction of high-affinity **ligands** from small mols. with much lower affinities. Computer-aided drug design uses building, linking, and/or rigid docking procedures to search for **ligands** for a certain binding site. Scoring functions provide a rank order of the designed **ligands** according to their estd. binding affinities. Further developments in computer-aided drug design are automated approaches for the flexible alignment of mols., the flexible docking of **ligands** to their binding sites, and the stepwise assembly of synthetically easily accessible **ligands** from **combinatorial libraries** of fragments.

L65 ANSWER 18 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:490658 HCAPLUS
DN 129:131265
TI Complexes and combinations of fetuin with therapeutic agents
IN Tracey, Kevin J.; Wang, Haichao
PA The Picower Institute for Medical Research, USA
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9830583	A1	19980716	WO 1998-US390	19980108 <--
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9860194	A1	19980803	AU 1998-60194	19980108 <--
	EP 971949	A1	20000119	EP 1998-903416	19980108 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	US 1997-780311		19970108 <--		
	WO 1998-US390		19980108 <--		

OS MARPAT 129:131265
AB A complex and a combination of the glycosylated **polypeptide** fetuin and a therapeutically active small mol. compd. having a net pos. charge at physiol. pH are disclosed. The presence of fetuin as a drug complex or in combination with the therapeutically active small mol. compd. enhances therapeutic activity of the small mol. compd. The invention further provides a means for screening for therapeutically active small mol. compds. by means of binding to fetuin. Low concns. of CNI-1493 were active in suppressing TNF prodn. in LPS-stimulated PBMCs, and this activity was enhanced by co-administration of human fetuin.

L65 ANSWER 19 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:485235 HCAPLUS
DN 129:106284
TI Method to classify gene products
IN Kauvar, Lawrence M.; Villar, Hugo O.

PA Terrapin Technologies, Inc., USA
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9829744	A2	19980709	WO 1997-US23762	19971223 <--
	WO 9829744	A3	19981112		
	W: AU, BA, CA, CU, GH, GM, GW, ID, IL, JP, LC, SL, YU, ZW				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9859020	A1	19980731	AU 1998-59020	19971223 <--
PRAI	US 1997-785360		19970103 <--		
	WO 1997-US23762		19971223 <--		

AB Methods for classifying large nos. of **proteins** contained in a collection of interest are described. The collection may represent the repertoire of **proteins** encoded by the genome of an organism including a higher organism or those expressed by a particular tissue or type of cell. Classification is based on ability to bind **ligands** contained in a panel representative of the range of physiol. interactions. The methods of the invention may also be used to evaluate relative binding of **proteins** in a set of **proteins** with respect to a physiol. significant **ligand** so as to permit the modification of specificity of a desired **ligand**/receptor interaction. For example, **protein** signatures are used in drug design for antiinfective agents.

L65 ANSWER 20 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:251322 HCAPLUS
DN 128:304032
TI System to detect small molecule/**peptide** interaction
IN Kauvar, Lawrence M.; Napolitano, Eugene W.
PA Terrapin Technologies, Inc., USA
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9816835	A2	19980423	WO 1997-US17975	19971003 <--
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5846722	A	19981208	US 1996-731613	19961016 <--
	AU 9748085	A1	19980511	AU 1997-48085	19971003 <--
PRAI	US 1996-731613		19961016 <--		
	WO 1997-US17975		19971003 <--		

AB Improved methods for detg. interactions between **peptides** or **proteins** and small mols. are disclosed. The invention methods can be used to screen **libraries** of either the small mols. or the **proteins**. In general, the methods comprise contacting an agent/**ligand** complex consisting essentially of an agent to be tested for binding to a target **protein** coupled to a **ligand** capable of binding a proteinaceous **ligand**-binding domain with a first fusion **protein** comprising said target **protein** and a first complementary portion of a segregable **protein**; and a second fusion **protein** comprising a proteinaceous **ligand** -binding domain and a second complementary portion of said segregable **protein**; and detecting whether the first complementary portion and second complementary portion are brought into proximity. The system is of use in drug discovery and development.

L65 ANSWER 21 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:119594 HCAPLUS
DN 128:238959

TI High-Affinity Aptamers Selectively Inhibit Human Nonpancreatic Secretory Phospholipase A2 (hnps-PLA2)
AU Bridonneau, Philippe; Chang, Ying-Fon; O'Connell, Dan; Gill, Stanley C.; Snyder, David W.; Johnson, Lea; Goodson, Theodore, Jr.; Herron, David K.; Parma, David H.
CS NeXstar Pharmaceuticals Inc., Boulder, CO, 80301, USA
SO J. Med. Chem. (**1998**), 41(6), 778-786
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB A family of sequence-related 2'-aminopyrimidine, 2'-hydroxylpurine aptamers, developed by oligonucleotide-based **combinatorial chem.**, SELEX (systematic evolution of **ligand** by exponential enrichment) technol., binds human nonpancreatic secretory phospholipase A2 (hnps-PLA2) with nanomolar affinities and inhibits enzymic activity. Aptamer 15, derived from the family, binds hnps-PLA2 with a Kd equal to 1.7 .+-. 0.2 nM and, in a std. chromogenic assay of enzymic activity, inhibits hnps-PLA2 with an IC50 of 4 nM, at a mole fraction of substrate concn. of 4 .times. 10-6 and a calcd. Ki of 0.14 nM. Aptamer 15 is selective for hnps-PLA2, having a 25- and 2500-fold lower affinity, resp., for the unrelated **proteins** human neutrophil elastase and human IgG. Contractions of guinea pig lung pleural strips induced by hnps-PLA2 are abolished by 0.3 .mu.M aptamer 15, whereas contractions induced by arachidonic acid are not altered. The structure that is essential for binding and inhibition appears to be a 40-base hairpin/loop motif with an asym. internal loop. The affinity and activity of the aptamers demonstrate the ability of the SELEX process to isolate antagonists of nonnucleic-acid-binding **proteins** from vast oligonucleotide **combinatorial libraries**.

L65 ANSWER 22 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:805891 HCAPLUS
DN 128:57436
TI A method for selecting target pathogen-inhibiting substances, and test kits for use therein
IN Lankinen, Hilkka; Heiskanen, Tuomas; Vaheri, Antti; Lundkvist, Ake
PA Helsinki University Licensing Ltd., Finland; Lankinen, Hilkka; Heiskanen, Tuomas; Vaheri, Antti; Lundkvist, Ake
SO PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9745743	A1	19971204	WO 1997-FI339	19970530 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	FI 9602269	A	19971201	FI 1996-2269	19960530 <--
	AU 9729650	A1	19980105	AU 1997-29650	19970530 <--
PRAI	FI 1996-2269		19960530 <--		
	WO 1997-FI339		19970530 <--		

AB A method is disclosed for selecting pathogen-inhibiting substances with high affinity and neutralizing effect by competitive elution using neutralizing substances. The method and system are useful for comparative drug design to provide therapeutically active, protective and/or prophylactic substances and developing **combinatorial** therapies as well as for pathogen diagnostics. The invention also discloses methods for identifying the mimotype characteristics of the neutralization site of

pathogens, esp. enveloped viruses, e.g. hantavirus or respiratory syncytial virus. The invention is further related to **ligands** obtainable by the method, as well as consensus sequences and parts and repeats of the **ligands** for use in test kits contg. **combinatorial ligand libraries** comprising the **ligands** selected by the method.

L65 ANSWER 23 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:746207 HCAPLUS
DN 128:20302
TI Microplate thermal shift assay and apparatus for **ligand** development and multi-variable **protein** chemistry optimization
IN Pantoliano, Michael W.; Rhind, Alexander W.; Salemme, Francis R.; Springer, Barry A.; Bone, Roger F.; Petrella, Eugenio C.
PA 3-Dimensional Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 175 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9742500	A1	19971113	WO 1997-US8154	19970509 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9732050	A1	19971126	AU 1997-32050	19970509 <--
	EP 914608	A1	19990512	EP 1997-927628	19970509 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 6020141	A	20000201	US 1997-853464	19970509 <--
	US 6036920	A	20000314	US 1997-853459	19970509 <--
	JP 2000511629	T2	20000905	JP 1997-540260	19970509 <--
	US 6232085	B1	20010515	US 1999-458691	19991210 <--
	US 6214293	B1	20010410	US 1999-459996	19991214 <--
PRAI	US 1996-17860	P	19960509 <--		
	US 1997-853459	A1	19970509 <--		
	US 1997-853464	A3	19970509 <--		
	WO 1997-US8154	W	19970509 <--		

AB The present invention is a method for ranking the affinity of each of a multiplicity of different mols. for a target mol. which is capable of denaturing due to a thermal change. The method comprises contacting the target mol. with one mol. of the multiplicity of different mols. in each of a multiplicity of containers, simultaneously heating the multiplicity of containers, measuring in each of the containers a phys. change assocd. with the thermal denaturation of the target mol. resulting from the heating in each of the containers, generating a thermal denaturation curve for the target mol. as a function of temp. for each of the containers and detg. a midpoint temp. (Tm) therefrom, comparing the Tm of each of the thermal denaturation curves with the Tm of a thermal denaturation curve obtained for the target mol. in the absence of any of the mols. in the multiplicity of different mols., and ranking the affinities of the multiplicity of different mols. according to the change in Tm of each of the thermal denaturation curves. The present invention also provides an assay app. that includes a temp.-adjusting means for simultaneously heating a plurality of samples, and a receiving means for receiving spectral emission from the samples while the samples are being heated. In further aspects of the invention, the receiving means can be configured to receive fluorescent emission, UV light, and visible light. The receiving means can be configured to receive spectral emission from the samples in a variety of ways, e.g., one sample at a time, simultaneously from >1

sample, or simultaneously from all of the samples. The temp.-adjusting means can be configured with a temp. controller for changing temp. in accordance with a predetd. profile.

L65 ANSWER 24 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:746070 HCAPLUS
DN 128:30375
TI Auto-deconvoluting **combinatorial libraries** of compounds interacting with enzymes, receptors, or other active moieties
IN Quibell, Martin; Johnson, Tony; Hart, Terance
PA Peptide Therapeutics Limited, UK; Quibell, Martin; Johnson, Tony; Hart, Terance
SO PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9742216	A1	19971113	WO 1997-GB1158	19970424 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2252408	AA	19971113	CA 1997-2252408	19970424 <--
	AU 9726450	A1	19971126	AU 1997-26450	19970424 <--
	AU 728263	B2	20010104		
	EP 906334	A1	19990407	EP 1997-918253	19970424 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2000512979	T2	20001003	JP 1997-539622	19970424 <--
PRAI	GB 1996-8457	A	19960424 <--		
	GB 1996-16115	A	19960731 <--		
	GB 1996-24584	A	19961127 <--		
	WO 1997-GB1158	W	19970424 <--		

AB The present invention relates to the field of app. (set of compds.) and methods which provide the rapid generation of structure/activity relationships using auto-deconvoluting **combinatorial libraries**, which facilitate the invention of novel active compds. The invention provides app. and methods which can be used for the rapid generation of structure/activity relationship (SAR) data, and, therefore, the characterization of the active motif of any group of compds. The invention provides **libraries** of compds. which interact with an active moiety, and app. and methods to identify such compds. The active moieties may be (but are not limited to) enzymes (e.g. kinases), receptors, antibodies, etc. The interaction of the active moiety with the compds. of the **library** may be (but is not limited to) the interaction of a substrate or inhibitor with an enzyme, the interaction of a **ligand** with a receptor, the interaction of an antigen or antigenic epitope with an antibody, etc. The invention describes e.g. the synthesis of a no. of compds. for use as a **library** for screening for potential substrates for dust mite Der P1 cysteine protease, as well as subsequent identification and synthesis of active inhibitors of the enzyme.

L65 ANSWER 25 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:740333 HCAPLUS
DN 128:10873
TI A three-hybrid reporter gene method for screening for **proteins** binding defined **ligands**
IN Liu, Jun; Licitra, Edward J.
PA Massachusetts Institute of Technology, USA

SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9741255	A1	19971106	WO 1997-US6912	19970425 <--
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2252886	AA	19971106	CA 1997-2252886	19970425 <--
EP 907750	A1	19990414	EP 1997-921370	19970425 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 5928868	A	19990727	US 1997-845674	19970425 <--
JP 2000508923	T2	20000718	JP 1997-539036	19970425 <--
PRAI US 1996-17341	P	19960426 <--		
WO 1997-US6912	W	19970425 <--		

AB A method for identifying the binding partner for a define **ligand** using an extension of the two-hybrid system is described. The method uses a fusion **protein** of the LexA **protein** and a **ligand** binding **protein** to bind to a LexA operator upstream of a reporter gene. This is bound to by a conjugate of the natural **ligand** for the **protein** and the **ligand** of interest. Possible binding partners for the **ligand** are identified by introduction of an expression **library** in which the **proteins** are synthesized as fusion products with a transcriptional activator. When the necessary combination of LexA fusion **protein** , **ligand**, and transcriptional activator fusion **protein** are brought together, the reporter gene is expressed. The method is particularly intended for the identification of natural binding partners for small mols. A fusion product of LexA and the rat glucocorticoid receptor is used in a reconstruction expt. with FK506-binding **protein** FKBP12 is used to demonstrate using a conjugate of dexamethasone and FK506 as the hybrid **ligand**.

L65 ANSWER 26 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:679258 HCAPLUS
DN 127:314806
TI Compositions and methods for screening drug **libraries**
IN Spinella, Dominic Gregory; Becherer, Kathleen Ann; Brown, Steven Joel
PA Chugai Biopharmaceuticals, Inc., USA
SO PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9737220	A1	19971009	WO 1997-US5821	19970402 <--
W: AU, CA, JP, KR				
US 5866341	A	19990202	US 1996-627151	19960403 <--
AU 9726619	A1	19971022	AU 1997-26619	19970402 <--
AU 717289	B2	20000323		
JP 2001503131	T2	20010306	JP 1997-535624	19970402 <--
EP 801307	A2	19971015	EP 1997-302302	19970403 <--
EP 801307	A3	19981216		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
PRAI US 1996-627151	A	19960403 <--		
WO 1997-US5821	W	19970402 <--		

AB A method of screening for binding partners of a specific mol. The method employs a chimeric **protein** having at least two different binding regions; one contg. at least a portion of the specific mol. or an analog thereof, and the other contg. a binding region of an Ig chain. In a preferred embodiment, the method is used for rapidly screening member compds. of a **combinatorial library** for potential biol.

activity.

L65 ANSWER 27 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:640834 HCAPLUS
DN 127:326501
TI Enantiomeric screening process and compositions therefor
IN Forster, Anthony C.
PA President and Fellows of Harvard College, USA; Forster, Anthony C.
SO PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9735194	A2	19970925	WO 1997-US4176	19970321 <--
	WO 9735194	A3	19971218		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9725313	A1	19971010	AU 1997-25313	19970321 <--
PRAI	US 1996-622338		19960321 <--		
	WO 1997-US4176		19970321 <--		

AB The present invention makes available a powerful directed approach for identifying enantioselective compds. which bind to biol. targets. The goal was to provide a method for **ligand** and drug discovery that may enable one to rapidly discover drug candidates for **protein** targets. As a general overview, the present invention relates, in one aspect, to a method for identifying compds. which interact with a target mol. by (1) contacting a screening mol. with a variegated compd. **library**, wherein the screening mol. comprises solid target mol. or the enantiomer thereof if the target mol. is chiral; (2) selecting from the **library** compds. which have a desired interaction with the target mol.; and (3) testing the ability of the enantiomer of a compd. selected in step (2) to interact with the target mol. The method was tested with 3 different drug targets and 2 different control targets, and the results presented support the feasibility of the method.

L65 ANSWER 28 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:594339 HCAPLUS
DN 127:287684
TI Use of the multiple copy simultaneous search (MCSS) method to design a new class of picornavirus capsid binding drugs
AU Joseph-Mccarthy, Diane; Hogle, James M.; Karplus, Martin
CS Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School, Boston, MA, 02115, USA
SO Proteins: Struct., Funct., Genet. (**1997**), 29(1), 32-58
CODEN: PSFGEY; ISSN: 0887-3585
PB Wiley-Liss
DT Journal
LA English
AB A **combinatorial ligand** design approach based on the multiple copy simultaneous search (MCSS) method and a simple scheme for joining MCSS functional group sites was applied to the binding pocket of P3/Sabin poliovirus and rhinovirus 14. The MCSS method dets. where specific functional (**chem.**) groups have local potential energy min. in the binding site. Before the virus application, test calcns. were run to det. the optimal set of input parameters to be used in evaluating the MCSS results. The MCSS min. are analyzed and selected min. are connected with (CH2)n linkers to form candidate **ligands**, whose structures are optimized in the binding site. Ests. of the binding

strength were made for the **ligands** and compared with those for known drugs. The results indicate that the proposed **ligands** should bind to P3/Sabin poliovirus at least as well as the best of the existing drugs, and that they should also bind to P1/Mahoney poliovirus and rhinovirus 14. A detailed comparison of the poliovirus and rhinovirus binding pockets and an anal. of drug binding specificity is presented.

L65 ANSWER 29 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:551555 HCAPLUS
DN 127:229143
TI Mass spectrometric identification of **ligands** selected from **combinatorial libraries** using gel filtration
AU Dunayevskiy, Yuriy M.; Lai, Jan-Ji; Quinn, Cheryl; Talley, Frank; Vouros, Paul
CS Barnett Institute and Department of Chemistry, Northeastern University, Boston, MA, USA
SO Rapid Commun. Mass Spectrom. (**1997**), 11(11), 1178-1184
CODEN: RCMSEF; ISSN: 0951-4198
PB Wiley
DT Journal
LA English
AB There is a const. search for a successful anal. methodol. to provide high throughput screening of **combinatorial libraries** against biol. targets for identification of active **ligands**. Solid-phase screening assays offer faster isolation and identification of active analytes compared to the soln.-based iterative methods. Shift of **combinatorial** research to the creation of sol. non-**peptide libraries**, and limitations assocd. with the heterogeneous assays, creates a demand for a breakthrough technol. for rapid and efficient screening of **combinatorial libraries** in soln. We demonstrated the efficient and rapid approach for selecting active **ligands** from a **combinatorial** mixt. with subsequent identification of compds. by mass spectrometry. The procedure involves the use of a biol. target mol. to phys. isolate the active component in a mixt. on a size exclusion medium. Then the **ligands** are identified using a combined liq. chromatog./capillary electrophoresis/mass spectrometry system. As a model system we used serum albumin and small mols. with different affinities to the **protein**.

L65 ANSWER 30 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:511999 HCAPLUS
DN 127:117370
TI Screening natural samples for new therapeutic and diagnostic compounds using capillary electrophoresis
IN Hughes, Dallas E.; Karger, Barry L.
PA Northeastern University, USA
SO PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9722000	A1	19970619	WO 1996-US19779	19961210 <--
	W: CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5783397	A	19980721	US 1996-662085	19960612 <--
	CA 2239418	AA	19970619	CA 1996-2239418	19961210 <--
	EP 876609	A1	19981111	EP 1996-944795	19961210 <--
	R: CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, IE				
	JP 2000502443	T2	20000229	JP 1997-522198	19961210 <--
PRAI	US 1995-8503		19951211 <--		
	US 1996-662085		19960612 <--		
	WO 1996-US19779		19961210 <--		

AB A method in which natural sample components are simultaneously fractionated and screened for compds. that bind tightly to specific mols.

of interest is disclosed. Such newly isolated **ligands** are good candidates for potential therapeutic or diagnostic compds. The natural sample is first combined with a potential target mol. and then subjected to capillary electrophoresis (CE). Charged (or even neutral) compds. present in the natural sample that bind to the added target mol. can alter its normal migration time upon CE, by changing its charge-to-mass ratio, or will cause a variation in peak shape or area. Complex formation can be detected by simply monitoring the migration of the target mol. during electrophoresis. Any new **ligands** that bind to the target mol. will be good candidates for therapeutic or diagnostic compds. Interfering, weak-binding **ligands** commonly present in crude exts. are not detected. Small, neutral **ligands**, as well as charged **ligands**, can be identified in competitive binding expts. with known, charged competitor mols.

L65 ANSWER 31 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:462958 HCAPLUS
DN 127:185250
TI Affinity selection and mass spectrometry-based strategies to identify lead compounds in **combinatorial libraries**
AU Kaur, Surinder; McGuire, Lisa; Tang, Dazhi; Dollinger, Gavin; Huebner, Verena
CS Protein Structure, Chiron Corp., Emeryville, CA, 94608-2916, USA
SO J. Protein Chem. (**1997**), 16(5), 505-511
CODEN: JPCHD2; ISSN: 0277-8033
PB Plenum
DT Journal
LA English
AB The screening of diverse **libraries** of small mols. created by **combinatorial** synthetic methods is a recent development which has the potential to accelerate the identification of lead compds. in drug discovery. We developed a direct and rapid method to identify lead compds. in **libraries** involving affinity selection and mass spectrometry. In our strategy, the receptor or target mol. of interest is used to isolate the active components from the **library** phys., followed by direct structural identification of the active compds. bound to the target mol. by mass spectrometry. In a drug design strategy, structurally diverse **libraries** can be used for the initial identification of lead compds. Once lead compds. have been identified, **libraries** contg. compds. **chem**. similar to the lead compd. can be generated and used to optimize the binding characteristics. These strategies have also been adopted for more detailed studies of **protein-ligand** interactions.

L65 ANSWER 32 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:414082 HCAPLUS
DN 127:103713
TI Bacteriophage display and discovery of **peptide** leads for drug development
AU Lowman, H. B.
CS Dep. Protein Eng., Genentech Inc., South San Francisco, CA, 94080, USA
SO Annu. Rev. Biophys. Biomol. Struct. (**1997**), 26, 401-424
CODEN: ABBSE4; ISSN: 1056-8700
PB Annual Reviews
DT Journal; General Review
LA English
AB A review with 67 refs. Phage display makes large-**peptide** diversity **libraries** readily attainable for identifying novel **peptide ligands** for receptors and other **protein** or non-**protein** targets. This technol. kindles enthusiasm for the idea that large and **protein-protein** interaction surfaces (epitopes) can be distd. down to small pharmacophores. These may be accessible to org. scaffolding, yielding new orally active drugs that might otherwise have taken greater time and effort to be discovered through chem.-**library** screening. This review, though not comprehensive with respect to the explosive vol. of phage display work

over the last few years, focuses on recent developments in phage-displayed **peptide** technol.

L65 ANSWER 33 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:414069 HCAPLUS
DN 127:105650
TI Structural and mechanistic determinants of affinity and specificity of **ligands** discovered or engineered by phage display
AU Katz, Bradley A.
CS Arris Pharmaceutical Corp., South San Francisco, CA, 94080, USA
SO Annu. Rev. Biophys. Biomol. Struct. (**1997**), 26, 27-45
CODEN: ABBSE4; ISSN: 1056-8700
PB Annual Reviews
DT Journal; General Review
LA English
AB A review with 98 refs. The scope and utility of phage display is reviewed with emphasis on medical applications and structure-based **ligand** and drug design, from literature mostly after 1994. General principles by which phage-displayed **peptides** achieve affinity and selectivity for targets are described, along with selected structural or mechanistic studies of the binding of **peptides** or **proteins** discovered or engineered by phage display. Such engineered **proteins** whose wild-type or mutant crystal or 2D-NMR structures yield insight about the basis for enhanced affinity or altered specificity include antibodies, zinc fingers, human growth hormone, **protein** A, and atrial natriuretic **peptide**. Structures of complexes of de novo phage-discovered **peptide ligands** with targets such as the Src SH3 domain, streptavidin, and erythropoietin receptor reveal the structural basis for receptor-**peptide** recognition in these systems.

L65 ANSWER 34 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:412422 HCAPLUS
DN 127:66175
TI New **ligands** for the human melanoma MSH receptor identified by a peptoid **library** (oligo N-substituted glycines)
AU Heizmann, Gerhard; Tanner, Heidi; Eberle, Alex N.
CS Laboratory of Endocrinology, Department of Research (ZLF), University Hospital and University Children's Hospital, Basel, CH-4031, Switz.
SO Innovation Perspect. Solid Phase Synth. Comb. Libr., Collect. Pap., Int. Symp., 4th (**1996**), Meeting Date 1995, 391-394. Editor(s): Epton, Roger. Publisher: Mayflower Scientific, Birmingham, UK.
CODEN: 64ONA9
DT Conference
LA English
AB A symposium report. A random peptoid **library** contg. 328,509 *single compds. with* **mol. wts.** *lower than* 850 Dalton was synthesized using the solid-phase sub-monomer approach and was tested for MSH receptor binding to human HBL melanoma cells in vitro. The deconvolution process to discover the active components of the **library**, originally introduced by R. A. Houghten et al. (1991), led to the identification of structurally new MSH receptor **ligands** with low **mol. wts.** and reasonable binding affinities. The dissocn. consts. of four of the tripeptoids ranged between 1.58 and 2.07 .mu.mol/l. Since this type of peptoid is known to display enhanced biostability, good hydrophilicity and biodistribution, the new MSH receptor **ligands** described here may represent novel leads for the development of diagnostic or therapeutic agents for human melanoma metastasis.

L65 ANSWER 35 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:412390 HCAPLUS
DN 127:75935
TI Solid phase synthesis of a directed small organic **library**: discovery of a new class of delta opioid drug lead
AU Letulle, Marguerite M.; Collins, Nathan; Davis, Peg; Knapp, Richard; Lee,

Kathy; Yamamura, Hank; Porreca, Frank; Hurby, Victor J.
CS Department of Chemistry, University of Arizona, Tucson, AZ, 85721, USA
SO Innovation Perspect. Solid Phase Synth. Comb. Libr., Collect. Pap., Int. Symp., 4th (**1996**), Meeting Date 1995, 281-284. Editor(s): Epton, Roger. Publisher: Mayflower Scientific, Birmingham, UK. CODEN: 64ONA9
DT Conference
LA English
AB Comparative mol. modeling of known delta and kappa **peptide** opioid **ligands** has led to the definition of the "message" and "address" binding sites and to the design of small peptidomimetic mols. predicted to be delta selective. The authors adopted a directed **combinatorial library** approach to assemble a variety of scaffolds displaying the message and address pharmacophores. Three scaffolds, 12 message moieties and 2 address moieties were chosen leading to a test **library** of 18 sublibraries (total **library** size = 120). Ex-vivo testing of these mixts. in mouse vas deferens and guinea pig ileum smooth muscle bioassays demonstrated delta affinity and selectivity in most cases. This has led to the discovery of a new class of delta opioid non-peptidic drug leads.

L65 ANSWER 36 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:366411 HCAPLUS
DN 126:325496
TI Anti-.alpha.-galactosyl epitope screening technique
IN Lussow, Alexander R.; Buelow, Roland; Pouletty, Philippe
PA Sangstat Medical Corporation, USA; Lussow, Alexander R.; Buelow, Roland; Pouletty, Philippe
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9715831	A1	19970501	WO 1996-US15448	19960927 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG				
	CA 2207760	AA	19970501	CA 1996-2207760	19960927 <--
	AU 9671689	A1	19970515	AU 1996-71689	19960927 <--
	AU 716818	B2	20000309		
	EP 799422	A1	19971008	EP 1996-933152	19960927 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 10510059	T2	19980929	JP 1996-516613	19960927 <--
PRAI	US 1995-6044	P	19951024 <--		
	WO 1996-US15448	W	19960927 <--		

AB Compds. and **libraries** are labeled with a galactosyl epitope and then screened in accordance with an assay involving cells having a characteristic of interest. Conveniently, the screening may embody target cells, where the compds. are brought in contact with the cells. Each of the compds. carries with it the information of its identity or method of synthesis. After washing away non-specifically bound compds., blood may be applied to the cells, whereby antibody binding to the galactosyl epitope initiates the complement cascade. Plaques are identified and the compd. assocd. with the plaque identified. The formation of the plaque demonstrates that the compd. has specific affinity for the target cell, binding of the compd. to the cell does not interfere with binding of the antibody, and that the complex is capable of cytotoxic activity by means of the complement cascade. The galactosyl-modified compds. specifically binding to a target can be used as cytotoxic drugs.

L65 ANSWER 37 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:363755 HCAPLUS
DN 127:92054
TI Structure-based design and **combinatorial chemistry** yield low nanomolar inhibitors of cathepsin D
AU Kick, Ellen K.; Roe, Diana C.; Skillman, A. Geoffrey; Liu, Guangcheng; Ewing, Todd, J. A.; Sun, Yaxiong; Kuntz, Irwin D.; Ellman, Jonathan A.
CS Dep. Chem., Univ. California, Berkeley, CA, 94720-4160, USA
SO Chem. Biol. (**1997**), 4(4), 297-307
CODEN: CBOLE2; ISSN: 1074-5521
PB Current Biology
DT Journal
LA English
AB The identification of potent small mol. **ligands** to receptors and enzymes is one of the major goals of **chem**. and biol. research. Two powerful new tools that can be used in these efforts are **combinatorial chem**. and structure-based design. Here we address how to join these methods in a design protocol that produces **libraries** of compds. that are directed against specific macromol. targets. The aspartyl class of proteases, which is involved in numerous biol. processes, was chosen to demonstrate this effective procedure. Using cathepsin D, a prototypical aspartyl protease, a no. of low nanomolar inhibitors were rapidly identified. Although cathepsin D is implicated in a no. of therapeutically relevant processes, potent nonpeptide inhibitors have not been reported previously. The **libraries**, synthesized on solid support, displayed nonpeptide functionality about the (hydroxyethyl)**amine** isostere. The (hydroxyethyl)**amine** isostere, which targets the aspartyl protease class, is a stable mimetic of the tetrahedral intermediate of **amide** hydrolysis. Structure-based design, using the crystal structure of cathepsin D complexed with the **peptide**-based natural product pepstatin, was used to select the building blocks for the **library** synthesis. The **library** yielded a 'hit rate' of 6-7% at 1 .mu.M inhibitor concns., with the most potent compd. having a Ki value of 73 nM. More potent, nonpeptide inhibitors (Ki = 9-15 nM) of cathepsin D were rapidly identified by synthesizing and screening a small second generation **library**. The success of these studies clearly demonstrates the power of coupling the complementary methods of **combinatorial chem**. and structure-based design. We anticipate that the general approaches described here will be successful for other members of the aspartyl protease class and for many other enzyme classes.

L65 ANSWER 38 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:141018 HCAPLUS
DN 126:139859
TI Method for discovery of **peptide** receptor agonists
IN Coughlin, Shaun R.; Chen, Ji; Bernstein, Harold; Ishii, Maki; Wang, Ling; Chen, Mian
PA Regents of the University of California, USA
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN:CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9641004	A1	19961219	WO 1996-US9176	19960604 <--
	W: CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5925529	A	19990720	US 1995-483506	19950607 <--
PRAI	US 1995-483506		19950607 <--		

AB The invention relates to **peptide ligand** discovery and is particularly directed to a method for the discovery of agonists for membrane bound receptors. The inventive detection system involves the use

of a "tethered" **ligand** for probing receptor binding. The general detection system comprises: a membrane, a membrane bound receptor, and a chimeric **ligand** presenting mol. This chimeric **protein** forms the tethered **ligand** and in turn comprises: a membrane domain, a linker domain, a **ligand** domain, and a cleavable terminal domain. The "**ligands**" of the system are exposed by the addn. of a specific peptidase that cleaves at the designated sequence. The sequence of the **ligand** that produces signal as a result of the interaction between the agonist and receptor can then be isolated using sib selection.

L65 ANSWER 39 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:50386 HCAPLUS
DN 126:152347
TI The measurement of molecular diversity: a three-dimensional approach
AU Chapman, David
CS Afferent Systems Inc., San Francisco, CA, 94114, USA
SO J. Comput.-Aided Mol. Des. (**1996**), 10(6), 501-512
CODEN: JCADEQ; ISSN: 0920-654X
PB ESCOM
DT Journal
LA English
AB This paper describes a method for selecting a small, highly diverse subset from a large pool of mols. The method has been employed in the design of **combinatorial** synthetic **libraries** for use in high-throughput screening for pharmaceutical lead generation. It computes diversity in terms of the main factors relevant to **ligand-protein** binding, namely the three-dimensional arrangement of steric bulk and of polar functionalities and mol. entropy. The method was used to select a set of 20 carboxylates suitable for use as side-chain **precursors** in a **polyamine**-based **library**. The method depends on ests. of various phys.-**chem**. parameters involved in **ligand-protein** binding; expts. examd. the sensitivity of the method to these parameters. This paper compares the diversity of randomly and rationally selected side-chain sets; the results suggest that careful design of synthetic **combinatorial** **libraries** may increase their effectiveness several-fold.

L65 ANSWER 40 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:32640 HCAPLUS
DN 126:69614
TI Evolutionary and genetic methods in drug design
AU Parrill, Abby L.
CS Department Chemistry, Michigan State University, East Lansing, MI, 48824, USA
SO Drug Discovery Today (**1996**), 1(12), 514-521
CODEN: DDTOFS; ISSN: 1359-6446
PB Elsevier
DT Journal; General Review
LA English
AB A review, with 60 refs. Many phases of rational drug design involve finding solns. to large combinatorial problems for which an exhaustive search is intractable. A simulation of the evolutionary pressure of natural selection can be incorporated into artificial intelligence algorithms to rapidly find good, if not optimal, solns. to such problems. This review describes implementations and select applications of genetic algorithms and evolutionary programming in various aspects of rational drug design. Evolutionary methods have been developed in the areas of pharmacophore elucidation, lead discovery and lead optimization, as well as in many areas of **peripheral** importance to rational drug design.

L65 ANSWER 41 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:529860 HCAPLUS
DN 125:188428
TI Secondary structure templated **libraries**: mimicking nature

AU Qabar, Maher; Urban, Jan; Sia, Charles; Klein, Michel; Kahn, Michael
CS Molecumetics Ltd., Bellevue, VA, 98005, USA
SO Mol. Diversity Comb. Chem.: Libr. Drug Discovery, Conf. (**1996**), 2-9. Editor(s): Chaiken, Irwin M.; Janda, Kim D. Publisher: American Chemical Society, Washington, D. C.
CODEN: 63HMAW
DT Conference; General Review
LA English
AB A review with 23 refs. Nature has used a "**library** approach" to constructing **ligands** for specific receptors and enzymes by combining a limited functional diversity of 20 **amino acid** side-chains with a small array of secondary structure motifs-reverse turns, .alpha.-helixes and .beta.-strands. The dissection of multidomain **proteins** into small synthetic conformationally restricted components is an important step in the design of low **mol. wt.** nonpeptides that mimic the activity of the native **protein**. Mimetics of crit. functional domains might possess beneficial properties in comparison to the intact proteinaceous species with regard to specificity and therapeutic potential. **Combinatorial** secondary structure templated **libraries** provide a powerful engine for the development of novel vaccines and pharmaceuticals.

L65 ANSWER 42 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:524186 HCAPLUS
DN 125:211649
TI Unraveling principles of lead discovery: From unfrustrated energy landscapes to novel molecular anchors
AU Rejto, Paul A.; Verkhivker, Gennady M.
CS Agouron Pharmaceuticals Inc., San Diego, CA, 92121, USA
SO Proc. Natl. Acad. Sci. U. S. A. (**1996**), 93(17), 8945-8950
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English
AB The search for novel leads is a crit. step in the drug discovery process. Computational approaches to identify new lead mols. have focused on discovering complete **ligands** by evaluating the binding affinity of a large no. of candidates, a task of considerable complexity. A new computational method is introduced in this work based on the premise that the primary mol. recognition event in the **protein** binding site may be accomplished by small core fragments that serve as mol. anchors, providing a structurally stable platform that can be subsequently tailored into complete **ligands**. To fulfill its role, we show that an effective mol. anchor must meet both the thermodn. requirement of relative energetic stability of a single binding mode and its consistent kinetic accessibility, which may be measured by the structural consensus of multiple docking simulations. From a large no. of candidates, this technique is able to identify known core fragments responsible for primary recognition by the FK506 binding **protein** (FKBP-12), along with a diverse repertoire of novel mol. cores. By contrast, abs. energetic criteria for selecting mol. anchors are found to be promiscuous. A relation between a min. frustration principle of binding energy landscapes and receptor-specific mol. anchors in their role as "recognition nuclei" is established, thereby unraveling a mechanism of lead discovery and providing a practical route to receptor-biased computational **combinatorial chem.**

L65 ANSWER 43 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:490626 HCAPLUS
DN 125:215413
TI Efficient vasoactive intestinal polypeptide hydrolyzing autoantibody light chains selected by phage display
AU Tyutyulkova, Sonia; Gao, Qing-Sheng; Thompson, Austin; Rennard, Steven; Paul, Sudhir
CS Departments of Anesthesiology, Internal Medicine and Eppley Cancer Research Institute, University of Nebraska Medical Center, 600 South 42nd

Street, Omaha, NE, 68198-6830, USA
SO Biochim. Biophys. Acta (**1996**), 1316(3), 217-223
CODEN: BBACAQ; ISSN: 0006-3002
DT Journal
LA English
AB An Ig light chain (L chain) library derived from the **peripheral** blood lymphocytes of a patient with asthma was cloned into a phagemid vector. Phage particles displaying L chains capable of binding vasoactive intestinal polypeptide (VIP) were isolated by affinity chromatog. Two VIP binding L chains were expressed in Escherichia coli in sol. form and purified to electrophoretic homogeneity by metal chelating and protein L affinity chromatog. Both L chains catalyzed the hydrolysis of [Tyr10-125I]VIP substrate. The catalytic activity eluted at the **mol. mass** of the monomer form of the L chain (28 kDa) from a gel filtration column. The activity was bound by immobilized anti-.kappa.-chain antibody. A control recombinant L chain displayed no catalytic activity. Hydrolysis of VIP by the catalytic L chains was saturable and consistent with Michaelis-Menten kinetics. The turnover of the L chains was moderate (0.22 and 2.21/min) and their Km values indicated comparatively high affinity recognition of VIP (111 and 202 nM), producing catalytic efficiencies comparable to or greater than trypsin. Unlike trypsin, the L chains did not display detectable cleavage of casein, suggesting a catalytic activity specialized for VIP. Comparisons of the nucleotide sequences of the L chain cDNA with their putative germ-line counterparts suggested the presence of several replacement mutations in the complementarity detg. regions (CDRs). These observations suggest: (a) Retention or acquisition of catalytic activity by the L chains is compatible with affinity maturation of antibodies; and (b) The autoimmune L chain repertoire can serve as a source of substrate-specific and efficient catalysts.

L65 ANSWER 44 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:416636 HCAPLUS
TI Chemical approach to understanding and controlling signal transduction.
AU Schreiber, Stuart L.
CS Department Chemistry and Chemical Biology, Cambridge, MA, 02138, USA
SO Book of Abstracts, 212th ACS National Meeting, Orlando, FL, August 25-29 (**1996**), BIOL-093 Publisher: American Chemical Society, Washington, D. C.
CODEN: 63BFAF
DT Conference; Meeting Abstract
LA English
AB Insights into signaling pathways and other cellular processes have resulted from studies of cell permeable, org. mols. identified from natural sources and designed and synthesized in the lab. This lecture will present results of studies using such mols. to understand and control intracellular signaling pathways - the **chem.** genetics approach. These low **mol. wt. ligands** cause either a conditional loss of function following binding to the products of wild type alleles or a gain of function following binding to the products of rationally designed conditional alleles. Examples are seen in studies of immunophilin-natural product complexes that led to the identification of calcineurin as a mediator of T cell receptor signaling and of FRAP as a mediator of signaling that links mitogenic pathways to the cell cycle machinery. A family of cell permeable **ligands** that induce intracellular **proteins** to assoc., developed in collaboration with Gerald Crabtree, has been used to regulate transcription and signal transduction (including pathways emanating from the T cell receptor and the apoptosis-inducing Fas antigen), and other cellular processes such as intracellular **protein** degrdn. and translocation. Finally, we have been using **protein**-structure-based **combinatorial** **chem.** to discover cell permeable **ligands** to any **protein** target. Such a capability is required in order for **chem.** genetics to have the broad generality of classical genetics-based methods for studying **protein** function.

L65 ANSWER 45 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:362839 HCAPLUS
DN 125:80901
TI Affinity purification of von Willebrand factor using **ligands** derived from **peptide libraries**
AU Huang, Ping Y.; Baumbach, George A.; Dadd, Christopher A.; Buettner, Joseph A.; Masecar, Barbara L.; Hentsch, Marc; Hammond, David J.; Carbonell, Ruben G.
CS Department Chemical Engineering, North Carolina State University, Raleigh, NC, 27695-7905, USA
SO Bioorg. Med. Chem. (**1996**), 4(5), 699-708
CODEN: BMECEP; ISSN: 0968-0896
DT Journal
LA English
AB The chromatog. purifn. of vWF (von Willebrand FActor) from human plasma represents a challenge because it consists of multimers with **mol**. **wts**. ranging from 0.5 to 10 million Daltons. Phage **peptide library** screening yielded a lead **peptide** (RLRSFY) that interacts with vWF. Conservative substitutions of terminal residues of the lead **peptide** led to a second **peptide**, RVRSFY, which was more efficient in the affinity chromatog. purifn. of vWF from **protein** mixts. Adsorption isotherm measurements indicated multiple interactions between vWF and the immobilized **peptide** RVRSFy. Increases in **peptide** d. on the chromatog. support resulted in stronger assocn. consts. and higher max. **protein** binding capacities. When the **peptide** d. was lower than 32 mg/mL, there was no measurable interaction between vWF and immobilized **peptide** RVRSFY in HEPES buffer contg. 0.5 M NaCl at pH 7. An increase in **peptide** d. from 32 to 60 mg/mL increased the assocn. consts. from 0.9 .times. 106 to 2 .times. 106 (M-1). Divalent salts (calcium and magnesium chloride) were used to elute the retained vWF with 82.5% of the activity recovered. The interactions between vWF and the immobilized **peptide** RVRSFY are dominated by ionic attractions and also involve hydrophobic interactions at close contact. Finally, the purifn. of vWF from crude material PEG filtrate of a cryoppt. of human plasma is demonstrated using affinity chromatog. with immobilized N-acetyl-RVRSFYK.

L65 ANSWER 46 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:290683 HCAPLUS
DN 125:29276
TI Electrospray mass spectrometry of biomacromolecular complexes with noncovalent interactions - new analytical perspectives for supramolecular chemistry and molecular recognition processes
AU Przybylski, Michael; Glocker, Michael O.
CS Fak. Chemie, Universitaet, Konstanz, D-78434, Germany
SO Angew. Chem., Int. Ed. Engl. (**1996**), 35(8), 806-826
CODEN: ACIEAY; ISSN: 0570-0833
DT Journal; General Review
LA English
AB A review with 185 refs. The development of "soft" ionization methods in recent years has enabled substantial progress in the mass spectrometric characterization of macromols., in particular important biopolymers such as **proteins** and nucleic acids. In contrast to the still existing limitations for the detn. of **mol**. **wts**. by other ionization methods such as fast atom bombardment and plasma desorption, electrospray ionization (ESI) and matrix-assisted laser desorption have provided a breakthrough to macromols. larger than 100 kDa. Whereas these methods have been successfully applied to det. the **mol**. **wt**. and primary structure of biopolymers, the recently discovered direct characterization by ESI-MS of complexes contg. noncovalent interactions ("noncovalent complexes") opens new perspectives for supramol. **chem**. and anal. biochem. Unlike other ionization methods ESI-MS can be performed in homogeneous soln. and under nearly physiol. conditions of pH, concn., and temp. ESI mass spectra of biopolymers, particularly **proteins**, exhibit series of multiply

charged macromol. ions with charge states and distributions ("charge structures") characteristic of structural states in soln., which enable a differentiation between native and denatured tertiary structures. In the first part of this article, fundamental principles, the present knowledge about ion formation mechanism(s) of ESI-MS, the relations between tertiary structures in soln. and charge structures of macro-ions in the gas phase, and exptl. preconditions for the identification of noncovalent complexes are described. The hitherto successful applications to the identification of enzyme-substrate and -inhibitor complexes, supramol. **protein** - and **protein**-nucleotide complexes, double-stranded polynucleotides, as well as synthetic self-assembled complexes demonstrate broad potential for the direct analyses if specific noncovalent interactions. The present results suggest new applications for the characterization of supramol. structures and mol. recognition processes that previously have not been amenable to mass spectrometry; for example, the sequence-specific oligomerization of **polypeptides**, antigen-antibody complexes, enzyme- and receptor-**ligand** interactions, and the evaluation of mol. specificity in **combinatorial** syntheses and self-assembled systems.

L65 ANSWER 47 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:241240 HCAPLUS
DN 124:306207
TI Pharmaceutical applications of peptidomimetics
AU Qabar, Maher; Urban, Jan; Sia, Charles; Klein, Michel; Kahn, Michael
CS Molumetrics Ltd., Bellevue, WA, 98006, USA
SO Lett. Pept. Sci. (**1996**), 3(1), 25-30
CODEN: LPSCEM; ISSN: 0929-5666
DT Journal; General Review
LA English
AB A review, with 24 refs. Nature has used a '**library** approach' to constructing **ligands** for specific receptors and enzymes by combining a limited functional diversity of 20 **amino acid** side chains with a small array of secondary structure motifs - reverse turns, .alpha.-helixes and .beta.-strands. The dissection of multidomain **proteins** into small synthetic conformationally restricted components is an important step in the design of low-**mol.-wt.** nonpeptides that mimic the activity of the native **protein**. Mimetics of crit. function domains might possess beneficial properties with regard to specificity and therapeutic potential compared to the intact proteinaceous species. **Combinatorial** secondary-structure-templated **libraries** provide a powerful engine for the development of a novel vaccines and pharmaceuticals.

L65 ANSWER 48 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:922067 HCAPLUS
DN 123:330857
TI Affinity methods for identifying inhibitors of molecular interactions mediated by SH3 domains
IN Rickles, Richard J.; Brugge, Joan S.; Botfield, Martyn C.; Zoller, Mark J.
PA Ariad Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9524419	A1	19950914	WO 1995-US3208	19950313 <--

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9521598 A1 19950925 AU 1995-21598 19950313 <--
EP 750630 A1 19970102 EP 1995-914721 19950313 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE
PRAI US 1994-209835 19940311 <--
US 1995-369832 19950106 <--
WO 1995-US3208 19950313 <--
AB Affinity methods for screening **peptides** that inhibit **protein-protein** interactions dependent upon SH3 domains are described for use in the development of therapeutic agents. The method can also be used to identify binding requirements for SH3-mediated interactions. The method has identified a no. of unexpected novel, specific, and strongly binding **peptides**. Methods including screening of a **combinatorial** phage display **library**, or use of GAL4 fusion **proteins** with VP16 or SH3 to regulate expression of a reporter gene are described.

L65 ANSWER 49 OF 49 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:471840 HCAPLUS
DN 123:278073
TI Construction and use of synthetic constructs encoding syndecan
IN Saunders, Scott; Bernfield, Merton; Kato, Masato
PA Children's Medical Center Corp., USA; Board of Trustees of the Leland Stanford Jr.
SO PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9500633	A2	19950105	WO 1994-US6920	19940617 <--
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5486599	A	19960123	US 1993-78683	19930617 <--
AU 9471129	A1	19950117	AU 1994-71129	19940617 <--
EP 705332	A1	19960410	EP 1994-920272	19940617 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				

PRAI US 1993-78683 19930617 <--
US 1989-331585 19890329 <--
US 1991-746797 19910812 <--
US 1991-757654 19910906 <--
US 1992-856869 19920324 <--
WO 1994-US6920 19940617 <--
AB A purified mammalian proteoglycan, and genetic information encoding such proteoglycans, having a core polypeptide **mol. wt.** of about 30 kD to about 35 kD, and comprising a hydrophilic amino terminal extracellular region, a hydrophilic carboxy terminal cytoplasmic region, a transmembrane hydrophobic region between said cytoplasmic and extracellular regions, a protease susceptible cleavage sequence extracellularly adjacent the transmembrane region of the peptide, and .gtoreq.1 glycosylation sites for attachment of a heparan sulfate chain to the extracellular region. The glycosylation site comprises a heparan sulfate attachment sequence represented by the formula: Xac-ZX-Ser-Gly-Ser-Gly, where Xac represents an amino acid residue having an acidic side chain, and Z represents form 1 to 10 amino acid residues. Addnl. peptides having this glycosylation site and genetic information useful for prepg. a no. of variations based on this glycosylation site are also provided. Mol. cloning of cDNA for syndecan-1 from NMuMG mouse mammary epithelial cells and uses of the sol. syndecan derivs. contg. the heparan sulfate attachment sites in construction of chimeric functional proteins are disclosed. Prepn. of syndecan-fibronectin chimera, syndecan-growth factor chimera, and syndecan-growth factor receptor chimera is also described.

=> d bib abs hitrn tot l94

L94 ANSWER 1 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 2001:195211 HCAPLUS
DN 134:237838
TI Improved preparation of **peptide** nucleic acid (PNA) **combinatorial libraries**
IN Cook, Phillip Dan; Kiely, John; Sprankle, Kelly
PA Isis Pharmaceuticals, Inc., USA
SO U.S., 32 pp., Cont.-in-part of U.S. 5,539,083.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	US 6204326	B1	20010320		US 1998-131270	19980807	<--
	US 5539083	A	19960723		US 1994-200742	19940223	<--
	CA 2183371	AA	19950831		CA 1995-2183371	19950222	<--
	JP 11209393	A2	19990803		JP 1998-322576	19950222	<--
	AT 185572	E	19991015		AT 1995-911848	19950222	<--
	US 5864010	A	19990126		US 1996-587648	19960117	<--
PRAI	US 1994-200742	A2	19940223	<--			
	JP 1995-522421	A3	19950222	<--			

AB New sub-monomer synthetic methods for the prepn. of **peptide** nucleic acid oligomeric structures are disclosed that provide for the synthesis of both predefined sequence **peptide** nucleic acid oligomers as well as random sequence **peptide** nucleic acid oligomers. Further these methods also provide for the incorporation of **peptide** nucleic acid units or strings of such units with **amino acids** or strings of **amino acids** in chimeric **peptide** nucleic acid-**amino acid** compds. Further disclosed are methods of making random **libraries** of **peptide** nucleic acids using the fully preformed monomers. Thus, a **combinatorial library** of chimeric **peptide** nucleic acid oligomers was prepd. using 1-[(N2-benzyloxycarbonyl-N6-benzyloxy-2-aminopurin-9-yl)acetyl]-3-oxomorpholine (I), 1-[(N6-benzyloxycarbonyladenin-9-yl)acetyl]-3-oxomorpholine (II), 1-[(N4-benzyloxycarbonylcytosin-1-yl)acetyl]-3-oxomorpholine (III), and 1-(thymin-1-ylacetyl)-2-oxomorpholine (IV), which involved coupling of IV to a MBHA resin, Mitsunobu reaction of the resulting resin-bound hydroxy adduct with (Boc)2NH using Ph3P and di-Et azodicarboxylate, random coupling of the resulting resin-bound **peptide** nucleic acid monomer with a mixt. of I, II, III, and IV followed by Mitsunobu reaction for converting the terminal hydroxy group to the terminal **amine** moieties, repeating the latter procedure for extension of backbone and addn. of further nucleoside bases to complete the oligomer of the desired length, addn. of a **peptide** to the **peptide** nucleic acid unit using std. solid phase Merrifield **peptide** synthesis, and cleavage of **peptide** nucleic acid oligomers from the resin.

IT **75-44-5**, Carbonic dichloride **98-88-4**, Benzoyl chloride **598-21-0**, Bromoacetyl bromide
RL: RCT (Reactant)
(improved prepn. of **peptide** nucleic acid (PNA) **combinatorial libraries**)

IT **75-36-5DP**, Acetyl chloride, resin-bound **598-21-0DP**, Bromoacetyl bromide, reaction product with MBHA resin
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(improved prepn. of **peptide** nucleic acid (PNA) **combinatorial libraries**)

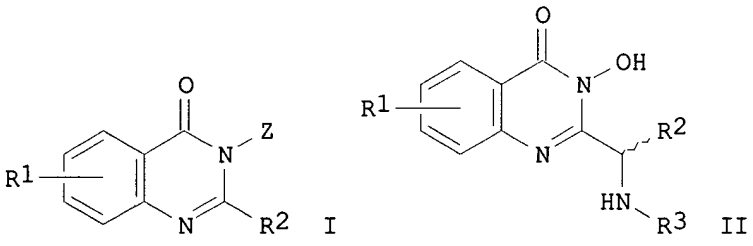
RE.CNT 28
RE
(1) Achari; Cold Spring Harbor Symp Quant Biol 1987, V52, P441 HCAPLUS

(2) Anon; WO 9119735 1991 HCAPLUS
(3) Anon; WO 9220702 1992 HCAPLUS
(4) Anon; WO 9220703 1992 HCAPLUS
(5) Anon; WO 9304204 1993 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L94 ANSWER 2 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 2001:91539 HCAPLUS
DN 134:147610
TI Compositions containing N-amino- and N-hydroxy-quinazolinones and methods for preparing **combinatorial libraries** thereof
IN Gao, Yun
PA Sepracor Inc., USA
SO U.S., 15 pp.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6184377	B1	20010206	US 1997-990855	19971215 <--

OS MARPAT 134:147610
GI



AB The invention is directed to certain N-amino- and N-hydroxy-quinazolinone compds., and methods for their synthesis. The compds. may find use in **combinatorial libraries**. More specifically, the invention is directed to the synthesis of 3-hydroxy- and 3-amino-4(1H)-quinazolinones via the reaction of an appropriate 2-aminobenzamide compd. with a carboxylic acid or acyl halide at ambient temp., performed on a solid support or in soln. In particular, the compds. are prepd. via supported compds. I [R1 = H, halo, alkyl, OH, alkoxy, etc.; or adjacent (R1)2 = (hetero)arom. fusion; R2 = (un)substituted alkyl, alkoxy, N-protected **amino acid** residue, Ph, etc.; Z = NHCO2CH2-Sup, OCH2-Sup, etc.; Sup = solid support]. For instance, Sup-ONH2 reacted with 15 isatoic anhydrides to give 15 supported 2-amino-N-hydroxybenzamides Sup-ONH-CO-C6H4-n(R1)n-NH2-2. The latter compds. were mixed into 5 groups of 3, and each group was then split 16 ways and cyclized sep. with each of 16 Fmoc-protected **amino acids**, using PyBrOP in DMAC as the condensing agent. Each of the 80 resultant Fmoc-protected quinazolinone mixts. was deprotected with piperidine, sepd. into 24 wells of a reactor block, and reacted with a selection of 8 chloroformates, 8 sulfonyl chlorides, and 8 isocyanates. The resulting 1920 product mixts. were treated with TFA to cleave the resin, yielding a **library** of 5760 different 3-hydroxyquinazolin-4-ones [II; R1 = H, Me, MeO, halo, and/or NO2; R2 = **amino acid** sidechain; R3 = other sidechain forming a carbamate, sulfonamide, or urea group], as 3-compd. mixts., which were stored for future bioassay.

IT **108-23-6**, Isopropyl chloroformate **543-27-1**, Isobutyl chloroformate **1885-14-9**, Phenyl chloroformate
RL: RCT (Reactant)
(starting material; methods for prepn. of N-amino- and

N-hydroxy-quinazolinones and **combinatorial libraries** thereof)
RE.CNT 19
RE
(1) Askin; US 5169952 1992 HCAPLUS
(2) Christie, R; J Chem Soc Perkin Trans I 1985, P2779 HCAPLUS
(4) Edwards; US 5164371 1992 HCAPLUS
(5) Ghelardoni, M; Annali di Chimica 1974, V64, P445 HCAPLUS
(6) Gordon, E; J Medicinal Chem 1994, V37(10), P1385 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L94 ANSWER 3 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:658521 HCAPLUS
DN 133:251873
TI Oligomeric compounds having nitrogen-containing linkages and **combinatorial libraries** thereof
IN Cook, Phillip Dan; Sanghvi, Yogesh S.; Kung, Pei Pei
PA ISIS Pharmaceuticals, Inc., USA
SO U.S., 46 pp., Cont.-in-part of U.S. 5,783,682.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 72

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 6121433	A	20000919	US 1996-669300	19960808	<--
	US 5138045	A	19920811	US 1990-558663	19900727	<--
	US 5223618	A	19930629	US 1990-566836	19900813	<--
	US 5378825	A	19950103	US 1991-703619	19910521	<--
	WO 9220822	A1	19921126	WO 1992-US4294	19920521	<--
	W: AU, BR, CA, FI, HU, JP, KR, NO, US					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE					
	US 5386023	A	19950131	US 1993-40903	19930331	<--
	US 5489677	A	19960206	US 1993-40526	19930331	<--
	US 5783682	A	19980721	US 1994-180124	19940111	<--
	US 5834607	A	19981110	US 1994-361858	19941222	<--
	WO 9518623	A1	19950713	WO 1995-US350	19950111	<--
	W: CA, JP, US					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	US 6232463	B1	20010515	US 1998-128508	19980804	<--
	US 6146829	A	20001114	US 1998-144611	19980831	<--
PRAI	US 1990-558663	A2	19900727	<--		
	US 1990-566836	A2	19900813	<--		
	US 1991-703619	A2	19910521	<--		
	WO 1992-US4294	A2	19920521	<--		
	US 1992-903160	B2	19920624	<--		
	US 1993-39846	B2	19930330	<--		
	US 1993-39979	B2	19930330	<--		
	US 1993-40526	A2	19930331	<--		
	US 1993-40903	A2	19930331	<--		
	US 1993-40933	B2	19930331	<--		
	US 1994-180124	A2	19940111	<--		
	WO 1995-US350	W	19950111	<--		
	US 1992-844845	A2	19920303	<--		
	US 1992-943516	B1	19920911	<--		
	US 1997-861306	A3	19970421	<--		
	US 1997-948151	A1	19971009	<--		

AB Novel N-contg. compds., and **libraries** thereof, are disclosed. The compds. have potential applications in diagnosis, therapy, biochem., etc. The compds. are oligomeric, and are based on nitrogen atoms which are joined together with spanner groups. The compds. also contain "letters", i.e., functional groups, that are attached to the nitrogen atoms, to the spanner groups, or both. The combination of nitrogen atoms, spanner groups, and letters, thereby render the compds. and **libraries** with diverse properties. Such properties include (no data) nuclease resistance, PLA2 inhibition, mRNA hybridization, and LTB4

inhibition. Generalized and prophetic synthetic methods are described, with some data for several synthetic intermediates. Deconvolution using the SURF method (synthetic unrandomization of randomized fragments) is described. Several highly generalized, oligomeric Markush structures are claimed, each having 1-90 monomer units.

IT **7693-46-1**, 4-Nitrophenyl chloroformate
RL: RCT (Reactant)
(starting material; prepn. of oligomeric N-contg. compds. and **combinatorial libraries** thereof)

RE.CNT 97
RE
(1) Abdel-Magid; Tetrahedron Letters 1990, V31, P5595 HCAPLUS
(2) Achari; Cold Spring Harbor Symp Quant Biol 1987, V52, P441 HCAPLUS
(3) Alul; Nucl Acids Res 1991, V19(7), P1527 HCAPLUS
(4) Anon; WO 8605518 1986 HCAPLUS
(5) Anon; WO 9119735 1991 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L94 ANSWER 4 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:622463 HCAPLUS
DN 133:217719
TI 3-(Cyclohexanoheteroarylidenyl)-2-indolinone **protein** tyrosine kinase inhibitors, and their therapeutic use
IN Tang, Peng Cho; Sun, Li; McMahon, Gerald; Blake, Robert A.
PA Sugen, Inc., USA
SO U.S., 61 pp., Cont. -in-part of U.S. Ser. No. 99,842.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE
PI	US 6114371	A	20000905		US 1998-190970	19981112 <--
	US 6130238	A	20001010		US 1998-99842	19980619 <--
PRAI	US 1997-50977	P	19970620	<--		
	US 1997-59384	P	19970919	<--		
	US 1998-99842	A2	19980619			
	US 1997-59544	P	19970919	<--		

OS CASREACT 133:217719; MARPAT 133:217719
AB 3-(Cyclohexano-heteroarylidenyl)-2-indolinone compds., and physiol. acceptable salts and prodrugs thereof, are disclosed which are expected to modulate the activity of **protein** tyrosine kinases and therefore to be useful in the prevention and treatment of **protein** tyrosine kinase-related cellular disorders (cancer, arthritis, restenosis, etc.).

IT **75-36-5**, Acetyl chloride **79-04-9**, Chloroacetyl chloride **141-75-3**, Butanoyl chloride **7790-94-5**, Chlorosulfonic acid
RL: RCT (Reactant)
(reaction; cyclohexanoheteroarylidenyl indolinone **protein** tyrosine kinase inhibitors, and therapeutic use)

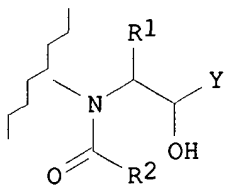
RE.CNT 38
RE
(1) Akbasak; J Neurol Sci 1992, V111, P119 HCAPLUS
(2) Andreani; Eur J Med Chem 1997, V32, P919 HCAPLUS
(3) Anon; WO 9115495 1991 HCAPLUS
(4) Anon; WO 9220642 1992 HCAPLUS
(5) Anon; WO 9221660 1992 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

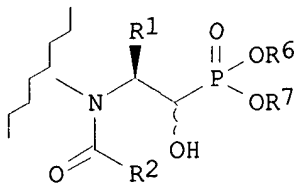
L94 ANSWER 5 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:704929 HCAPLUS
DN 131:322217
TI **Combinatorial amide** alcohol **libraries**
IN Dolle, Roland Ellwood, III; Herpin, Timothee Felix; Shimshock, Yvonne Class; Cavallaro, Cullen Lee
PA Pharmacopeia, Inc., USA

SO U.S., 34 pp.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5976894	A	19991102	US 1997-843214	19970414 <--

OS CASREACT 131:322217; MARPAT 131:322217
GI

Z = 

Z' = 

AB **Combinatorial chem. libraries** of the formula (T-L)q-[S]-CO-L'-Z (I), which include dihyroxy **amides** and hydroxyphosphonate **amides**, are disclosed [in which T = identifier residue; L = linker; q = 0-30; [S] = solid support; L' = linker; Z = ligand as shown; R1 = hydrocarbyl, substituted aryl or aralkyl, (CH2)nNHCOR3; R2 = hydrocarbyl, substituted alkyl, aryl, heteroaryl, or CHR4OCONHR3; R3 = hydrocarbyl, aryl; R4 = alkyl, aryl; n = 1-4; Y = PO3H2 esters, allyl, CH2CH(OH)CH2OH, CH2CHO, CH2CH2OH, (un)substituted CH2CH2OCONH2 or CH2CH2NH2]. The **combinatorial libraries** are optionally encoded with tags. The use of these **libraries** in assays to discover biol. active compds. is also disclosed. Prepns. of a 3255-member **library**, four 465-member **libraries**, a 23,250-member **library**, and a 24,180-member **library**, are described, as well as encoding and decoding procedures. For instance, TentaGel.RTM. resin was coupled with bis-Fmoc-lysine, encoded in 15 sep. batches, coupled with a photolinker, and then with 15 O-protected amino alcs. The 15 batches of resin were then mixed and split into 31 batches, which were coupled with either (1) 27 **acid chlorides**, or (2) ClCH2COOCH(CHMe2)COCl, followed by removal of the chloroacetyl group and coupling with 4 isocyanates. The 31 batches were combined, and the alc. functions were then deprotected, oxidized to the aldehyde, and coupled with a variety of compds. For instance, splitting of the resin into 7 batches and reaction with 7 phosphites gave a 3255-member **library** I [Z = Z' as shown; R1 = various natural and unnatural **amino acid** sidechains; R2 = various carboxylic acid-derived sidechains; R6, R7 = Me, Et, Bu, PhCH2, CH2CF3, CH2CH2Cl; or R6R7 = CH2CH2] in 7 sublibraries.
IT **98-88-4**, Benzoyl chloride **142-61-0**, Hexanoyl chloride **701-99-5**, Phenoxyacetyl chloride
RL: RCT (Reactant)
(starting material; prepn. of **amide**-alc. **combinatorial libraries**)
RE.CNT 9
RE
(1) Anon; WO 9306121 1993 HCAPLUS
(2) Baldwin; J Am Chem Soc 1995, V117, P5588 HCAPLUS
(3) Gordon; J Med Chem 1994, V37, P1385 HCAPLUS
(4) Kick; J Med Chem 1995, V38, P1427 HCAPLUS
(5) Murphy; J Am Chem Soc 1995, V117, P7029 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L94 ANSWER 6 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:655997 HCAPLUS
DN 131:243534

TI **Combinatorial** synthesis of **amino acid**
-containing thiosaccharides as antibacterial agents
IN Hindsgaul, Ole
PA Sunsorb Biotech, Inc., Can.
SO U.S., 36 pp., Cont.-in-part of U.S. 5,780,603.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 8

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5965719	A	19991012	US 1997-971222	19971114 <--
US 5780603	A	19980714	US 1996-751231	19961115 <--
PRAI US 1996-751231	A2	19961115 <--		

OS MARPAT 131:243534
AB Combinatorial synthesis of **amino acid**-contg. thiosaccharides AYCHR1(CHR3)nCHR2XR4 (A = saccharide; R1-R3 = independently H, alkyl, substituted alkyl, alkenyl, alkaryl, aryl, cycloalkyl, cycloalkenyl, heteroaryl, heterocyclic, thioalkoxyalkyl or joined together to form cycloalkyl, cycloalkenyl, heterocyclic ring; R4 = H, alkyl; X = O, S, SO, SO2, **amide**, acyl; Y = S, SO, SO2; n = 0, 1) optionally attached to a solid support, is reported. Thus, 2-hydroxycyclohex-1-yl 1-thio-.beta.-D-galactopyranoside was prepd. as inhibitor of heat labile enterotoxin and cholera toxin binding to ganglioside GD1b by at least 20%.
IT **112-16-3**, Lauroyl chloride
RL: RCT (Reactant)
(prepn. and **combinatorial libraries** of antibacterial **amino acid**-contg. thio glycosides)
RE.CNT 28
RE
(1) Anon; EP 0063373 1986 HCAPLUS
(3) Anon; WO 9306121 1993 HCAPLUS
(4) Anon; WO 9419360 1994 HCAPLUS
(5) Anon; EP 0649021 A1 1995 HCAPLUS
(6) Anon; WO 9521628 1995 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L94 ANSWER 7 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:425786 HCAPLUS
DN 131:74624
TI Preparation of functionalized crosslinked non(meth)acrylic polymer composites as solid supports for chemical **library** synthesis
IN Pears, David Alan; Denton, Bruce John
PA Zeneca Limited, UK
SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9932508	A1	19990701	WO 1998-GB3732	19981217 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9915697	A1	19990712	AU 1999-15697	19981217 <--
EP 1042357	A1	20001011	EP 1998-960006	19981217 <--
R: CH, DE, ES, FR, GB, IT, LI, NL				
PRAI GB 1997-27126	A	19971222 <--		
WO 1998-GB3732	W	19981217		

AB The laminar solid support material having good mech. and resilience is prepd. by polymg. a non(meth)acrylate monomer, oligomer or monomer/oligomer mixt. in a planar inert porous noncellulosic solid substrate under conditions that the non(meth)acrylate monomer, oligomer or monomer/oligomer mixt. is unreactive towards the substrate. Thus, chloromethylstyrene (40/60 mixt. of 3 and 4 isomers) 11.7, styrene 7.5 and divinylbenzene 0.4 g are reacted in the presence of 0.4 g AIBN at 60.degree. for 2 h, mixed with 0.4 g Me Et peroxide and 2 drops cobalt octoate, immediately coated onto a Leutrasil VS 3450 mat (thermally bonded polypropylene spunweb), continuously polymd. at room temp. and washed with THF to give a polymer composite.

IT **75-36-5DP**, Acetyl chloride, reaction products with benzhydryl derivs. of crosslinked polystyrene **100-07-2DP**, 4-Anisoyl chloride, reaction products with crosslinked polystyrene
RL: IMF (Industrial manufacture); RCT (Reactant); PREP (Preparation)
(prepn. of **library** of compds. by using functionalized crosslinked non(meth)acrylic polymer composites supports)

IT **98-88-4**, Benzoyl chloride
RL: RCT (Reactant)
(prepn. of **library** of compds. by using functionalized crosslinked non(meth)acrylic polymer composites supports)

RE.CNT 8

RE

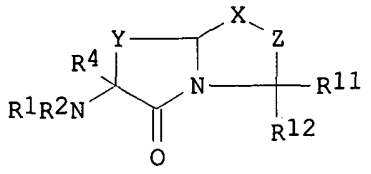
(1) Algemene, K; DE 1153526 B 1963 HCAPLUS
(2) Forskningscenter Risq; WO 9002749 A 1990 HCAPLUS
(4) Nisshinbo Industries Inc; EP 0710666 A 1996 HCAPLUS
(5) Pfizer Ltd; WO 9616078 A 1996 HCAPLUS
(6) Regents Of The University Of Minnesota; EP 0687691 A 1995 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

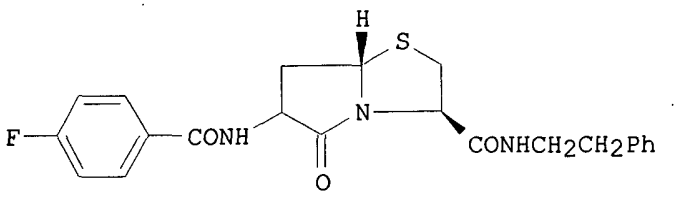
L94 ANSWER 8 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:405170 HCAPLUS
DN 131:45109
TI Peptidomimetic template-based **combinatorial libraries**
IN Cwi, Cynthia Lynn; Scott, William Leonard
PA Eli Lilly and Company, USA
SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9931507	A1	19990624	WO 1998-US26387	19981211 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9919102	A1	19990705	AU 1999-19102	19981211 <--
PRAI	US 1997-68025	P	19971218 <--		
	WO 1998-US26387	W	19981211		

OS MARPAT 131:45109
GI



I



II

AB Combinatorial arrays of lactam derivs. I [X = O, S, N, CR7R8 (R7, R8 = H or an electron-withdrawing substituent selected from hydroxyl, alkoxy, **amine**, thiol, carboxamido and alkyl); Y = (CR5R6)m and Z = (CR9 R10)n, where m and n are 1-4 and R5, R6, R9, R10 are H, alkyl, cycloalkyl, halo, hydroxy, oxo, thiol, sulfinyl, sulfonyl, amino, thiol, carbonyl, aryl, heterocyclyl; R1 = H, alkyl; R2 = H, alkyl, cycloalkyl, carbonyl, aryl, heterocyclyl, an **amino acid** residue, an N-protected **peptide** residue; R11 and R12 = H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heterocyclyl or R11 and R12 together with the nitrogen and ring carbon comprise an **amino acid** residue or C-protected **peptide** residue], which are useful for screening for therapeutically useful compds., were prepd. from resin-bound aldehydic **amino acid** intermediates. Thus, bicyclic compd. II was prepd. from allylglycine and showed 43% inhibition of influenza polymerase in vitro at a concn. of 10 .mu.M.

IT **403-43-0**, p-Fluorobenzoyl chloride
RL: RCT (Reactant)
(peptidomimetic template-based **combinatorial libraries**)

RE.CNT 8

RE

(1) Allen; Tetrahedron 1989, V45(7), P1905 HCAPLUS
(2) Baldwin; Heterocycles 1992, V34(5), P903 HCAPLUS
(3) Baldwin; Tetrahedron 1989, V45(14), P4537 HCAPLUS
(4) Baldwin; Tetrahedron Lett 1986, V27(30), P3461 HCAPLUS
(5) Moss; J Med Chem 1996, V39(11), P2178 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L94 ANSWER 9 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:405169 HCAPLUS
DN 131:44731
TI Parallel solution phase synthesis of lactams
IN Cwi, Cynthia Lynn; Scott, William Leonard
PA Eli Lilly and Company, USA
SO PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DT **Patent**
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9931506	A1	19990624	WO 1998-US25798	19981208 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9916277	A1	19990705	AU 1999-16277	19981208 <--
PRAI	US 1997-68027	P	19971218 <--		
	WO 1998-US25798	W	19981208		

OS MARPAT 131:44731

AB The present invention provides a parallel soln. phase process for making combinatorial arrays of lactam derivs., which are useful for screening for therapeutically useful compds. Thus, 8 aldehydes were reacted with 12 **amines** in MeOH in 4 mL screw-cap vials arranged on an 8.times.12 grid to form imines, and then CH2Cl2 was added, followed by Amberlite IRA 400 borohydride resin and aldehyde resin scavenger. The mixts. were shaken at room temp. overnight, filtered, and then heated at 60.degree. overnight to yield the lactam products. Yields were 50-100%.

IT **100-07-2**, p-Anisoyl chloride **103-80-0**, Phenylacetyl chloride **638-29-9**, Valeryl chloride **645-45-4**, Hydrocinnamoyl chloride **701-99-5**, Phenoxyacetyl chloride **2719-27-9**, Cyclohexanecarbonyl chloride **21615-34-9**, o-Anisoyl chloride
RL: RCT (Reactant)
(soln. phase combinatorial prepn. of lactams)

RE.CNT 10

RE

(1) Allen; Tetrahedron 1989, V45(7), P1905 HCAPLUS
(2) Baldwin; Heterocycles 1992, V34(5), P903 HCAPLUS
(4) Baldwin; Tetrahedron Lett 1986, V27(30), P3461 HCAPLUS
(5) Carporale; US 5767238 A 1998 HCAPLUS
(7) Kaldor; Tetrahedron Lett 1996, V37(40), P7193 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L94 ANSWER 10 OF 83 HCAPLUS COPYRIGHT 2001 ACS

AN 1999:271373 HCAPLUS

DN 130:282365

TI Coding **combinatorial libraries** with fluorine tags

IN Hochlowski, Jill E.; Sowin, Thomas J.; Norbeck, Daniel W.; Wade, Warren S.; Whittern, David N.

PA Abbott Laboratories, USA

SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2

DT **Patent**

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9919344	A1	19990422	WO 1998-US21408	19981009 <--
	W: CA, JP, MX				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 6168913	B1	20010102	US 1997-949987	19971014 <--
	EP 1023317	A1	20000802	EP 1998-953379	19981009 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
PRAI	US 1997-949987	A	19971014 <--		
	WO 1998-US21408	W	19981009		

AB The present invention relates to coding **combinatorial chem. libraries** synthesized on a plurality of solid

supports by attaching "tags" that comprise fluorine contg. compds. in combinations and/or ratios. The tags can be decoded while attached to the solid support by fluorine NMR spectroscopy to follow the reaction history of individual beads, and to det. the particular member of the **library** that is attached on the bead. Thus, coupling of Boc-Lys(Fmoc)-OH (Boc = Me3CO2C; Fmoc = 9-fluorenylmethoxycarbonyl) to (aminomethyl)polystyrene, followed by Fmoc deprotection and attachment of fluorine tag 3-(4-fluorophenyl)propionic acid gave tagged resin with a 19F NMR peak at -118 ppm. Other resins contg. 3,5-difluorophenylacetic acid, 4-(trifluoromethyl)benzoic acid, and 4-(trifluoromethoxy)benzoic acid were prepd., and showed 19F NMR peaks at -110, -63, and -58 ppm, resp. The tagged resins were split and pooled in defined coding ratios, linker 4-[4-(hydroxymethyl)phenoxy]butyric acid attached, and a coded, Fmoc-protected **amino acid** residue attached. The resins were pooled and split again, followed by deprotection and sulfonylation with alkyl and arom. sulfonyl chlorides. The resulting sulfonated **amino acid** resins were pooled and split a third time, followed by deprotonation and alkylation with alkyl bromides. Addnl. methods for attaching fluorine labels to solid-phase synthesis resins are also described.

RE.CNT 3
RE
(1) Abbott Laboratories; WO 9811036 A 1998 HCAPLUS
(2) Curagen Corporation; WO 9630849 A 1996 HCAPLUS
(3) Geysen, H; Current Biology 1996, V3(8), P679 HCAPLUS

L94 ANSWER 11 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:271361 HCAPLUS
DN 130:282174
TI Combined generation of phosphinic acid derivatives
IN Haaf, Klaus; Patek, Marcel
PA Hoechst Schering Agrevo G.m.b.H., Germany
SO PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DT **Patent**
LA German
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9919332	A1	19990422	WO 1998-EP6162	19980929 <--
	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	DE 19745628	A1	19990415	DE 1997-19745628	19971010 <--
	AU 9894421	A1	19990503	AU 1998-94421	19980929 <--
	EP 1023299	A1	20000802	EP 1998-947555	19980929 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL				
	ZA 9809181	A	19990409	ZA 1998-9181	19981008 <--
PRAI	US 1997-61619	P	19971009 <--		
	DE 1997-19745628	A	19971010 <--		
	WO 1998-EP6162	W	19980929		

AB Solid-phase-bound processes are disclosed for the systematic prepn. of chem. compds. from the group of the phosphinic or phosphonous acids or their derivs., and corresponding substance **libraries** which can be used for test purposes, in particular tests for biol. effects. Compds. YR1P(:O)(OR3)R2 (I; R1 = (un)substituted arom. or heteroarom. group; R2 = H, hetero atom contg. org. group; R3 = H, C-atom bonded org. group; Y = functional group from which the polymer resin can be easily cleaved), prepd. by reacting a resin linker addn. product [resin polymer]-[linker-Z-E1-S1]n with a phosphinate A1-O-(PHO)A*, in the presence of a suitable Pd catalyst, causing the substitution of group S1 and yielding [resin polymer]-[linker-Z-E1-P(H)(:O)-OA1], and after

resin-bound derivatization reactions, by sepg. the title compd. from the resin-linker addn. product. Also disclosed are the intermediate steps and resin-bound intermediate compds., as well as the resultant substance **libraries**. Thus, reaction of 4-iodobenzoic acid with hydroxy Wang polystyrene resin in the presence of dimethylaminopyridine/diisopropylcarbodiimide in CH2Cl2 gave 82.2% Wang-polystyrene-resin- bound 4-iodobenzoyloxy compd. which on phosphination with phosphoric acid followed by esterification gave Wang polystyrene resin bound 4-(ethoxyphosphinoyl)benzyloxy compd. Reaction of Wang-polystyrene-resin-bound 4-(ethoxyphosphinoyl)benzyloxy compd. with aldehydes, isocyanates, imines, alkenes, and org. halides gave title compds. as plant growth regulator material.

IT **79-30-1**, Isobutyric **acid chloride**
RL: RCT (Reactant)
(reaction with Wang polystyrene resin bound amino(iodobenzyloxy) compd.)

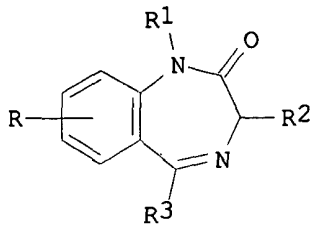
IT **28920-43-6D**, reaction products with Rink resin
RL: RCT (Reactant)
(reaction with iodobenzoic acid)

RE.CNT 5
RE
(1) Boyd, E; Tetrahedron Letters 1996, V37(10), P1647 HCAPLUS
(2) Cao, X; Tetrahedron Letters 1996, V37(34), P6073 HCAPLUS
(3) Dorff, P; Tetrahedron Letters 1998, V39(21), P3375 HCAPLUS
(4) Fruchtel, J; Angewandte Chemie. International Edition 1996, V35(1), P17
(5) Hoechst AG; DE 2346657 A 1975 HCAPLUS

L94 ANSWER 12 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:271341 HCAPLUS
DN 130:296702
TI Preparation of benzodiazepinones as **protein** tyrosine kinase inhibitors
IN Budde, Raymond J. A.; Ellman, Jonathan A.; Levin, Victor A.; Gallick, Gary E.; Newman, Robert A.
PA Board of Regents, the University of Texas System, USA; The Regents of the University of California
SO PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9919306	A2	19990422	WO 1998-US21327	19981009 <--
	WO 9919306	A3	19990729		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6100254	A	20000808	US 1997-948839	19971010 <--
	AU 9897950	A1	19990503	AU 1998-97950	19981009 <--
PRAI	US 1997-948839	A1	19971010 <--		
	WO 1998-US21327	W	19981009		

OS MARPAT 130:296702
GI



I

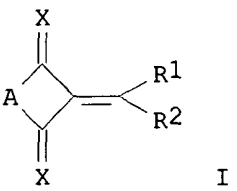
AB Title compds. [I; R = H, halo, alkyl, alkoxy, etc.; R1-R3 = YW; Y = bond or divalent group; W = H, (OX)azolyl, azinyl, etc.] were prepd. Thus, prepn. of I [R = 7-Cl, R1 = 4-PhC6H4CH2, R2 = CH2C6H4(OH)-4, R3 = C6H4(OH)-4] was described. Data for biol. activity of I were given.

IT **28920-43-6**
RL: RCT (Reactant)
(prepn. of benzodiazepinones as **protein** tyrosine kinase inhibitors)

L94 ANSWER 13 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:222923 HCAPLUS
DN 130:252372
TI Preparation of cyclic compounds as protecting and linking groups for organic synthesis.
IN Toth, Istvan; Dekany, Gyula; Kellam, Barry
PA Alchemia Pty. Ltd., Australia
SO PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9915510	A1	19990401	WO 1998-AU808	19980924 <--
	W: AU, CA, CN, HU, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9893303	A1	19990412	AU 1998-93303	19980924 <--
	EP 1017683	A1	20000712	EP 1998-946145	19980924 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	AU 1997-9375	A	19970924 <--		
	US 1997-61987	P	19971014 <--		
	WO 1998-AU808	W	19980924		

OS CASREACT 130:252372; MARPAT 130:252372
GI



I

AB Title compds. [I; A = atoms to form a (substituted) cycloalkyl, cycloheteroalkyl, bicyclyl, heterobicyclyl, tricyclyl, heterotricyclyl; X = O, S, (substituted) imino; R1 = H, (substituted) alkyl, alkenyl, alkynyl, heteroalkyl, aryl, heteroaryl, cycloalkyl, heterocycloalkyl, alkanal, thioalkanal, amino, guanidino, cyano, ammonio, CO2H, etc.; R2 = (substituted) alkylamino, dialkylamino, arylamino, diarylamino,

O-substituted hydroxylamino, hydrazido, thiohydrazido, semicarbazido, alkoxy, acyloxy, alkylthio, etc.; with a proviso], and related compds. were prepd. as protecting and linking groups for use in the synthesis of **peptides**, oligosaccharides, glycopeptides and glycolipids. I are useful in both solid phase and soln. synthesis, and are particularly applicable to combinatorial synthesis. Thus, 1,3-dimethylbarbituric acid and 4-dimethylaminopyridine in CH2Cl2 at 0.degree. were treated with PhCOCl over 15 min. followed by 3 h stirring at room temp. to give 64% 5-benzoyl-1,3-dimethyl-2,4,6(1H,3H,5H)-pyrimidinetrione. The latter was refluxed overnight with benzyl 2-amino-2-deoxy-.alpha.-D-glucopyranoside (II) and (Me2CH)2NEt in EtOH to give 71% benzyl 2-deoxy-2-[1-(1,3-dimethyl-2,4,6(1H,3H,5H)-trioxopyrimidin-5-ylidene)phenylmethylamino]-.alpha.-D-glucopyranoside. The latter was stirred with BuNH2 for 30 min. to give 92% II.

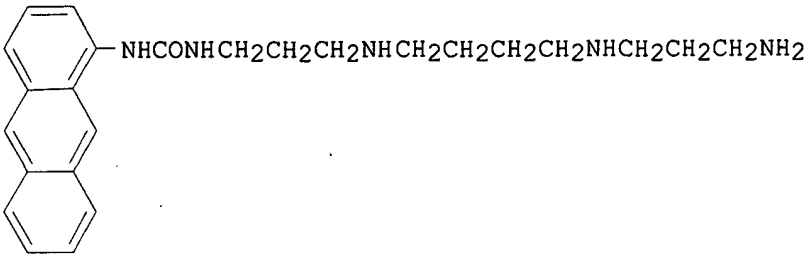
IT **98-88-4**, Benzoyl chloride **3282-30-2**, Pivaloyl chloride
RL: RCT (Reactant)
(prepn. of cyclic compds. as protecting and linking groups for org. synthesis)

RE.CNT 12
RE
(2) Alchemia Pty Ltd; WO 9838197 1998 HCAPLUS
(3) Alonso, G; Eur J Med Chem-Chimica Therapeutica 1978, V13(2), P155 HCAPLUS
(4) Bycroft, B; J Am Chem Soc 1994, V116, P7415 HCAPLUS
(7) Chan, W; Proc Eur Pept Symp 1995 HCAPLUS
(8) Chemipro Kasei Kaisha Ltd; WO 9814423 1998 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L94 ANSWER 14 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:77533 HCAPLUS
DN 130:153469
TI Novel polyamine analogs as therapeutic and diagnostic agents
IN Vermeulin, Nicolaas M. J.; O'Day, Christine L.; Webb, Heather K.; Burns, Mark R.; Bergstrom, Donald E.
PA Oridigm Corporation, USA
SO PCT Int. Appl., 143 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9903823	A2	19990128	WO 1998-US14896	19980715 <--
	WO 9903823	A3	19990408		
	W: AL, AM, AU, AZ, BA, BB, BG, BR, CA, CN, CU, CZ, EE, FI, GE, HU, IL, IS, JP, KG, KP, KR, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9884968	A1	19990210	AU 1998-84968	19980715 <--
	EP 1001927	A2	20000524	EP 1998-935790	19980715 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 6172261	B1	20010109	US 1999-341400	19990903 <--
PRAI	US 1997-52586	P	19970715 <--		
	US 1997-65728	P	19971114 <--		
	US 1998-85538	P	19980515		
	WO 1998-US14896	W	19980715		

OS MARPAT 130:153469
GI



I

AB Title inhibitors RXR1 [R =H, or is a head group consisting of a straight or branched C1-10 aliph., alicyclic, single or multiring arom., single or multiring aryl substituted aliph., etc.; R1 is a polyamine; X = CO, NHCO, NHCS, SO2] and pharmaceutical acceptable salts of polyamine transport having inhibition consts. two orders of magnitude lower than those of known compds. are disclosed. These polyamine analogs are useful pharmaceutical agents for treating diseases where it is desired to inhibit polyamine transport or other polyamine binding proteins, for example cancer and post-angioplasty injury and the introduction of a 3-amidopropyl group to the diaminobutyl part of spermidine produce a significantly better transport inhibitor. Novel **chem**. synthetic methods to obtain polyamine analogs are disclosed, including the prodn. of a **combinatorial** polyamine **library**. These approaches yield analogs with desirable activities both for diagnostic and research assays and therapy. The assays of the invention are useful for **high throughput** screening of targets in the discovery of drugs that interact with the polyamine system. Thus, I was prepd. from 1-aminoanthracene, 4-nitrophenyl chloroformate, and spermine.

IT **7693-46-1 28920-43-6**
RL: RCT (Reactant)
(prepn. of polyamines as therapeutic and diagnostic agents)

L94 ANSWER 15 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:45211 HCAPLUS
DN 130:110408
TI Preparation of fluorous silicon, tin and germanium compounds and their use in organic synthesis to facilitate organic/fluorous extractive purification
IN Curran, Dennis P.; Hadida, Ruah Sabine; Hoshino, Masahide; Studer, Armido; Wipf, Peter; Jeger, Patrick; Kim, Sun-young; Ferritto, Rafael
PA University of Pittsburgh, USA
SO U.S., 40 pp., Cont.-in-part of U.S. 5,777,121.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5859247	A	19990112	US 1996-690491	19960731 <--
	US 5777121	A	19980707	US 1996-671945	19960628 <--
	CA 2259183	AA	19980108	CA 1997-2259183	19970626 <--
	WO 9800376	A1	19980108	WO 1997-US11215	19970626 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9735818	A1	19980121	AU 1997-35818	19970626 <--
	EP 907625	A1	19990414	EP 1997-932333	19970626 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, FI

	JP 2000514062	T2	20001024	JP 1998-504319	19970626 <--
	US 6156896	A	20001205	US 1998-80274	19980515 <--
PRAI	US 1996-671945	A2	19960628 <--		
	US 1996-690491	A	19960731 <--		
	WO 1997-US11215	W	19970626 <--		

OS CASREACT 130:110408; MARPAT 130:110408

AB There is claimed a method of sepn. performed on a mixt. comprising at least a 1st org. compd. and a 2nd org. compd., the method comprising the steps of: a. selectively reacting the 1st org. compd. with a fluorous reaction component to attach a fluorous moiety to the 1st org. compd. to result in a fluorous compd., the fluorous moiety comprising sufficient F to render the fluorous compd. separable from the 2nd org. compd. via an org./fluorous phase sepn. technique; b. sepg. the fluorous compd. from the 2nd org. compd. via the org./fluorous phase sepn. technique. Several methods of synthesis (e.g. tin hydride reductive addn., reductive cyclization, ionic redns. of aldehydes; Stille couplings; prepn. of isoxazolines and isoxazoles by Mukaiyama's and Huisgen's methods; Grignard reaction/silylation; radical addn. and hydrostannylation; 1,3-dipolar cycloaddn. and hydrostannylation; prepn. of 5-substituted tetrazoles; Ugi-four-component condensation; and Biginelli reactions to give tetrahydropyrimidinecarboxylic acid esters) and sepn. are described in which org./fluorous phase sepn. techniques were used to effect sepns. An example application comprises adding nitroethane (0.44 mmol), Ph isocyanate (0.88 mmol) and 2 drops of Et3N to a soln. of allyl tris(2-(perfluorohexyl)ethyl)silyl ether (0.044 mmol) in benzotrifluoride (4 mL) and stirring at 25.degree. for 3 d; after removal of the solvent, the residue was purified by 3-phase extn. with FC-72 (20 mL), H2O (20 mL), and benzene (20 mL); the org.-aq. biphase was addnl. extd. twice with FC-72 (20 mL) to give 99% of 3-methyl-5-tris[2-(perfluorohexyl)ethyl]silyloxymethyl-4,5-dihydroisoxazole. The present invention also provides novel compns. of matter comprising fluorous Si, Sn and Ge compds. XM[(R)(Rf)]3, wherein X is H, F, Cl, Br, I, N3, OR1, OH, OOH, OOR1, SR1, SeR1, CN, NC, NR1R2, a cyclic group, a heterocyclic group, a linear or branched alkyl group of 1 to 20 carbons, an alkenyl group, an alkynyl group, an acyl group, M'((R')(Rf'))3, OM'((R')(Rf'))3 or OOM'((R')(Rf'))3, wherein M' is Si, Ge, or Sn, and wherein R1 and R2 are each independently the same or different H, a linear or branched alkyl group, a cyclic alkyl group, an alkylsulfonyloxy group, a perfluoroalkylsulfonyloxy group, an acyl group, or a perfluoroacyloxy group, and wherein M is Si, Ge or Sn, and wherein R and R' are each independently the same or different an alkylene group of 1 to 6 carbons and wherein Rf and Rf' are each independently a linear perfluoroalkyl group of 3 to 20 carbons, a branched perfluoroalkyl group of 3 to 20 carbons, or a hydrofluoroalkyl group of 3 to 20 carbons, the hydrofluoroalkyl group comprising up to one hydrogen atom for each two fluorine atoms.

IT **586-75-4P**, 4-Bromobenzoyl chloride
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction with propanethiol in presence of aluminum chloride in prepn. of tri-Pr 4-bromoorthothiobenzoate)

RE.CNT 23

RE

(2) Billiet; J of Chromotogaphy 1981, V218, P443 HCAPLUS
(3) Boutevin; US 5453528 1995 HCAPLUS
(4) Boutevin; J of Fluorine Chemistry 1993, V60, P211 HCAPLUS
(5) Boutevin; J of Fluorine Chemistry 1994, V68, P71 HCAPLUS
(8) Gladysz; Science 1994, V266, P55 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L94 ANSWER 16 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:747594 HCAPLUS
DN 130:22238
TI Enzymic ribozyme treatment of diseases or cancers related to expression of c-raf gene
IN Jarvis, Thale; Matulic-Adamic, Jasenka; Reynolds, Mark; Kisich, Kevin;

Bellon, Laurent; Parry, Tom; Beigelman, Leonid; McSwiggen, James A.; Karpeisky, Alexander; Burgin, Alex; Thompson, James; Workman, Christopher T.; Beaudry, Amber; Sweedler, David
PA Ribozyme Pharmaceuticals, Inc., USA; et al.
SO PCT Int. Appl., 259 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 3

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9850530	A2	19981112	WO 1998-US9249	19980505 <--
WO 9850530	A3	19990729		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9872905	A1	19981127	AU 1998-72905	19980505 <--
EP 980424	A2	20000223	EP 1998-920299	19980505 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6054576	A	20000425	US 1998-164964	19981001 <--
US 6162909	A	20001219	US 1999-326154	19990604 <--
PRAI US 1997-46059	P	19970509 <--		
US 1997-49002	P	19970609 <--		
US 1997-51718	P	19970703 <--		
US 1997-56808	P	19970822 <--		
US 1997-61321	P	19971002 <--		
US 1997-61324	P	19971002 <--		
US 1997-64866	P	19971105 <--		
US 1997-68212	P	19971219 <--		
WO 1998-US9249	W	19980505		
US 1998-164964	A1	19981001		

OS MARPAT 130:22238
AB This invention relates to identification, synthesis and use of nucleic acid catalysts to cleave RNA species that are required for cellular growth responses. In particular, the invention describes the selection and function of ribozymes capable of cleaving RNA encoded by c-raf gene. Such ribozymes may be used to inhibit the proliferation of tumor cells in one or more cancers, restenosis, psoriasis, fibrosis and rheumatoid arthritis.
IT **10025-87-3**, Phosphorus oxychloride
RL: RCT (Reactant)
(enzymic ribozyme treatment of diseases or cancers related to expression of c-raf gene)

L94 ANSWER 17 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:735078 HCAPLUS
DN 129:343727
TI Use of (cyanomethylene)phosphoranes as carbonyl 1,1-dipole synthons in constructing **combinatorial libraries**
IN Wasserman, Harry H.; Ho, Wen-Bin
PA Yale University, USA
SO U.S., 10 pp.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5834588	A	19981110	US 1995-503070	19950714 <--

OS CASREACT 129:343727; MARPAT 129:343727
AB The invention is directed to systematic synthetic and testing strategies

for .alpha.-keto acids, esters and **amides**. The method of synthesis comprises (A) reacting (cyanomethylene)triphenylphosphorane (I) with a carbonyl compd. selected from carboxylic acids (RCO2H) and acyl chlorides (RCOCl) to make a cyano(keto)phosphorane, (B) oxidizing said phosphorane, and (C) reacting the oxidized product with a nucleophile (NuH) to make the product .alpha.-keto acid, ester, or **amide**. Systematic synthesis and testing are achieved by a modular approach in which arrays of mols. are generated by variation of R and Nu. Thus, condensation of benzoyl chloride with I in the presence of bis(trimethylsilyl)acetamide in CH2Cl2 gave 95% adduct PhCOC(CN):PPh3 (II). Ozonolysis of II in CH2Cl2 at -78.degree., followed by addn. of H-Phe-OEt in CH2Cl2 gave 92% .alpha.-keto **amide** PhCOCO-Phe-OEt.

IT **98-88-4**, Benzoyl chloride
RL: RCT (Reactant)
((cyanomethylene)phosphoranes as carbonyl 1,1-dipole synthons for use in constructing **combinatorial libraries**)

L94 ANSWER 18 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:719165 HCAPLUS
DN 129:331055
TI Improved preparation of oligomeric **peptide** nucleic acid (PNA) **combinatorial libraries**
IN Cook, Phillip Dan; Kiely, John; Sprankle, Kelly
PA Isis Pharmaceuticals Inc, USA
SO U.S., 33 pp. Cont.-in-part of U.S. 5,539,083.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5831014	A	19981103	US 1996-693144	19960813 <--
	US 5539083	A	19960723	US 1994-200742	19940223 <--
	WO 9523163	A1	19950831	WO 1995-US2182	19950222 <--
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	JP 11209393	A2	19990803	JP 1998-322576	19950222 <--
PRAI	US 1994-200742	A2	19940223 <--		
	WO 1995-US2182	W	19950222 <--		
	JP 1995-522421	A3	19950222 <--		

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB New sub-monomer synthetic methods for the prepn. of **peptide** nucleic acid oligomeric structures are disclosed that provide for the synthesis of both predefined sequence **peptide** nucleic acid oligomers as well as random sequence **peptide** nucleic acid oligomers. Further these methods also provide for the incorporation of **peptide** nucleic acid units or strings of such units with **amino acids** or strings of **amino acids** in chimeric **peptide** nucleic acid-**amino acid** compds. Further disclosed are methods of making random **libraries** of **peptide** nucleic acids using the fully preformed monomers. Thus, a **combinatorial library** of chimeric **peptide** nucleic acid oligomers was prepd. using protected 2-oxomorphilone building blocks I-IV, which involved coupling of IV to a MBHA resin, Mitsunobu reaction of the resulting resin-bound hydroxy adduct

with (Boc)2NH using Ph3P and di-Et azodicarboxylate, random coupling of the resulting resin-bound **peptide** nucleic acid monomer with a mixt. of I, II, III, and IV followed by Mitsunobu reaction for converting the terminal hydroxy group to the terminal **amine** moieties, repeating the latter procedure for extension of backbone and addn. of further nucleoside bases to complete the oligomer of the desired length, addn. of a **peptide** to the **peptide** nucleic acid unit using std. solid phase Merrifield **peptide** synthesis, and cleavage of **peptide** nucleic acid oligomers from the resin.

IT **75-44-5**, Carbonic dichloride **98-88-4**, Benzoyl chloride **598-21-0**, Bromoacetyl bromide
RL: RCT (Reactant)
(improved prepn. of oligomeric **peptide** nucleic acid (PNA) **combinatorial libraries**)

IT **75-36-5DP**, Acetyl chloride, resin-bound **598-21-0DP**, Bromoacetyl bromide, reaction product with MBHA resin
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(improved prepn. of oligomeric **peptide** nucleic acid (PNA) **combinatorial libraries**)

L94 ANSWER 19 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:712381 HCAPLUS
DN 129:313134
TI **Combinatorial libraries** of peptidomimetic aminothioether acids
IN Mendel, David
PA Eli Lilly and Co., USA
SO PCT Int. Appl., 125 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

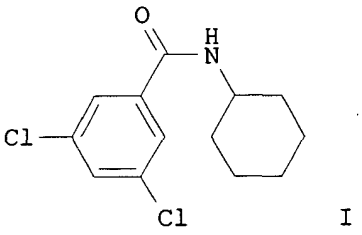
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9846786	A1	19981022	WO 1998-US7151	19980408 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9869620	A1	19981111	AU 1998-69620	19980408 <--
	EP 973936	A1	20000126	EP 1998-915437	19980408 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
PRAI	US 1997-43496		19970411 <--		
	WO 1998-US7151		19980408		

OS MARPAT 129:313134
AB The present invention relates to a novel diverse **library** of aminothioether compds. and derivs. thereof, and their possible use as lead compds. in drug development. Methods are presented for the prepn. of these peptidomimetic compds. The general method used to prep. the diverse **libraries** of amino thioether acid compds. utilizes com. available or readily synthesized **amino acids** or amino alcs. and mercapto acids. An app. providing a readily accessible source of individual members of the **library** is also described. The app. can be used in assay kits and as a replaceable element in automated assay machines.

IT **28920-43-6**
RL: RCT (Reactant)
(**combinatorial libraries** of peptidomimetic aminothioether acids)

L94 ANSWER 20 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:680439 HCAPLUS

DN 130:95100
TI Impurity annihilation; a strategy for solution phase **combinatorial chemistry** with minimal purification
AU Barrett, Anthony G. M.; Smith, Marie L.; Zecri, Frederic J.
CS Department of Chemistry, Imperial College of Science, Technology and Medicine, London, SW7 2AY, UK
SO Chem. Commun. (Cambridge) (**1998**), (21), 2317-2318
CODEN: CHCOFS; ISSN:.1359-7345
PB Royal Society of Chemistry
DT Journal
LA English
OS CASREACT 130:95100
GI



I

AB The selective annihilation of all contaminants in the soln. phase formation of **amides** or sulfonamides is accomplished by their incorporation into a polyurea and removal by filtration. E.g., **amide** I is prepd. in 96% yield and 99% purity by addn. of 3 equiv. of c-C6H11NH2 to 3,5-Cl2C6H3COCl in CH2Cl2 followed by the addn. of 3 equiv. of H2N(CH2CH2NH)4CH2CH2NH2, stirring for 40 min., and the addn. of 6 equiv. of 4-OCNC6H4NCO to form a ppt. which is filtered to give a soln. contg. I. **Amines** can be acylated with sepn. from acyl or sulfonyl chloride reactants as well by impurity annihilation. E.g., 2-MeOC6H4CH2NH2 is acylated with 4-MeC6H4SO2Cl (TsCl) in the presence of poly(vinylpyridine) in CH2Cl2; the addn. of 3 equiv. H2N(CH2CH2NH)4CH2CH2NH2 , stirring, and the addn. of 4-OCNC6H4NCO to yield a ppt. contg. two polymers which are filtered off to give a soln. contg. TsNHCH2C6H4-2-OMe in 84% yield and 92% purity.
IT **527-69-5**, 2-Furancarbonyl chloride **2719-27-9**, Cyclohexanecarbonyl chloride
RL: RCT (Reactant)
(prepn. and simplified purifn. of **amides** and sulfonamides by incorporation of excess reagents into a polyurea as a strategy for soln. phase combinatorial synthesis)
RE.CNT 25
RE
(1) Armstrong, R; Acc Chem Res 1996, V29, P123 HCAPLUS
(3) Booth, R; J Am Chem Soc 1997, V119, P4882 HCAPLUS
(4) Curran, D; Angew Chem Int Ed Engl 1998, V37, P1175 HCAPLUS
(5) Curran, D; J Am Chem Soc 1996, V118, P2531 HCAPLUS
(6) Dewitt, S; Acc Chem Res 1996, V29, P114 HCAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L94 ANSWER 21 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:660150 HCAPLUS
DN 129:330924
TI Solid-phase extraction on C18 silica as a purification strategy in the solution synthesis of a 1-thio-.beta.-D-galactopyranoside **library**
AU Nilsson, Ulf J.; Fournier, Eric J.-L.; Hindsgaul, Ole
CS Department of Chemistry, University of Alberta, Edmonton, T6G 2G2, Can.
SO Bioorg. Med. Chem. (**1998**), 6(9), 1563-1575
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Science Ltd.
DT Journal

LA English
AB A novel strategy for the purifn. of carbohydrate-based **chem. libraries** synthesized in soln. was developed. Purifn. of reaction products was accomplished by means of solid-phase extn. enabled by protecting the 2-, 3-, 4-, and 6-hydroxyl groups of a galactose deriv. as their hydrophobic O-laurates. The presence of multiple O-laurates allowed adsorption of reaction products onto C18 silica while reagents and byproducts were washed away with MeOH. Products were quant. eluted with pentane. Purifn. of products using solid-phase extn. offers the combined advantages of soln. synthesis (normal soln. reactivity and ease of reaction monitoring) with those of solid-phase synthesis (facile product isolation permitting the use of large excesses of reagents). To demonstrate the utility of the hydrophobic recovery-procedure, tetra-O-lauroyl-.beta.-D-galactopyranose-1-thiol was subjected to high-yielding reactions with a panel of Michael-acceptors and an .alpha.-chloro ketone. The resulting ketone adducts were then either reduced to the alcs. or reductively aminated with a selection of **amino acids** to give 30 different 1-thio-.beta.-D-galactosides as mixts. of four diastereomers after removal of protecting groups. At each step, the product was sepd. from the reagents and their byproducts by simple adsorption onto C18 silica, washing with MeOH and elution of product with pentane. After completion of the **combinatorial chem.** sequence, the O-laurates were cleaved by methanolysis and the product Me laurate in turn removed from the desired water-sol. products by C18 adsorption. Individual **library** members were thus conveniently produced on 10-30 mg scales at purity levels of >90%. One of the 1-thio-.beta.-D-galactosides thus produced was found to be a competitive inhibitor of the .beta.-galactosidase from E. coli with Ki value of 1.7 .mu.M.
IT **112-16-3**, Lauroyl chloride
RL: RCT (Reactant)
(solid-phase extn. on C18 silica as a purifn. strategy in the soln. synthesis of a 1-thio-.beta.-D-galactopyranoside **library**)

L94 ANSWER 22 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:630458 HCAPLUS
DN 129:330308
TI Chemically tagged Mitsunobu reagents for use in solution-phase chemical **library** synthesis
AU Starkey, Gale W.; Parlow, John J.; Flynn, Daniel L.
CS Parallel Medicinal Combinatorial Chemistry Unit, Searle Discovery Research, Monsanto Life Sciences Company-U2E, Saint Louis, MO, 63167, USA
SO Bioorg. Med. Chem. Lett. (**1998**), 8(17), 2385-2390
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
AB A general method for **high-throughput** product purifn. of Mitsunobu reactions is described. Tert-Bu ester-tagged phosphine and azodicarboxylate reagents, Ph2PCH2CH2CO2CMe3 and Me3CO2CCH2NHCON:NCONHCH2CO2CMe3, are used to synthesize individual **library** members in soln.-phase. Workup and purifn. are easily accomplished by post-reaction sequestration of the tagged reagents and reagent byproducts by a complementary functionalized ion exchange resin. The reagents are utilized in a 3 step **library** synthesis.
IT **98-88-4**, Benzoyl chloride **645-45-4**, 3-Phenylpropionyl chloride
RL: RCT (Reactant)
(chem. tagged Mitsunobu reagents for use in soln.-phase chem. **library** synthesis)

L94 ANSWER 23 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:624893 HCAPLUS
DN 129:316200
TI Novel safety-catch linker and its application with a Ugi/De-BOC/cyclization (UDC) strategy to access carboxylic acids,

1,4-benzodiazepines, diketopiperazines, ketopiperazines and dihydroquinoxalinones

AU Hulme, Christopher; Peng, John; Morton, George; Salvino, Joseph M.; Herpin, Tim; Labaudiniere, Richard

CS Rhone-Poulenc Rorer Cent. Res., Collegeville, PA, 19426, USA

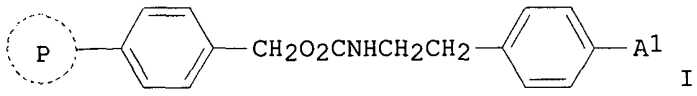
SO Tetrahedron Lett. (**1998**), 39(40), 7227-7230
CODEN: TELEAY; ISSN: 0040-4039

PB Elsevier Science Ltd.

DT Journal

LA English

GI



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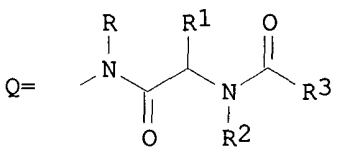

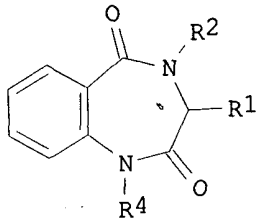

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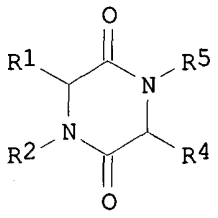
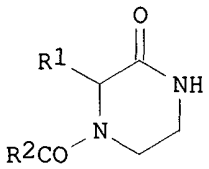
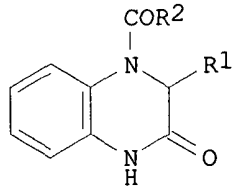


III



IV



V

AB This communication reveals the synthesis and application of a novel resin bound isonitrile (I; A1 = isocyano; P = Wang resin) which can be used for automated parallel synthesis of diverse arrays of compds. in **combinatorial chem.** The resin is an example of a novel safety-catch linker which upon BOC-activation can be resin cleaved with a variety of nucleophiles. Use of this polymer supported isonitrile in the Ugi multi-component reaction (MCR) with aldehydes R1CHO (R1 = unspecified aldehyde residue), **amines** R2NH2 (R2 = unspecified **amine** residue), and carboxylic acids R3CO2H (R3 = unspecified carboxylic acid residue) to form resin-bound Ugi products I (A1 = Q, R = H) followed by Boc-activation to I (A1 = Q, R = Boc) (i.e. safety catch) and resin clipping and cyclization. allows access to diverse arrays of 1,4-benzodiazepine-2,5-diones (II; R4 = unspecified substituent), diketopiperazines (III), ketopiperazines (IV), and dihydroquinoxalines (V), resp., as well as carboxylic acids (**amino acids**) (HO-Q) or their esters. The methoxide safety-catch clipping strategy and subsequent soln. phase cyclization. offers similar advantages to a traceless linker.

IT **7693-46-1**, 4-Nitrophenyl chloroformate
RL: RCT (Reactant)
(safety-catch linker resin and its application with Ugi/De-BOC/cyclization strategy to access carboxylic acids, benzodiazepines, diketopiperazines, ketopiperazines and dihydroquinoxalinones)

L94 ANSWER 24 OF 83 HCAPLUS COPYRIGHT 2001 ACS

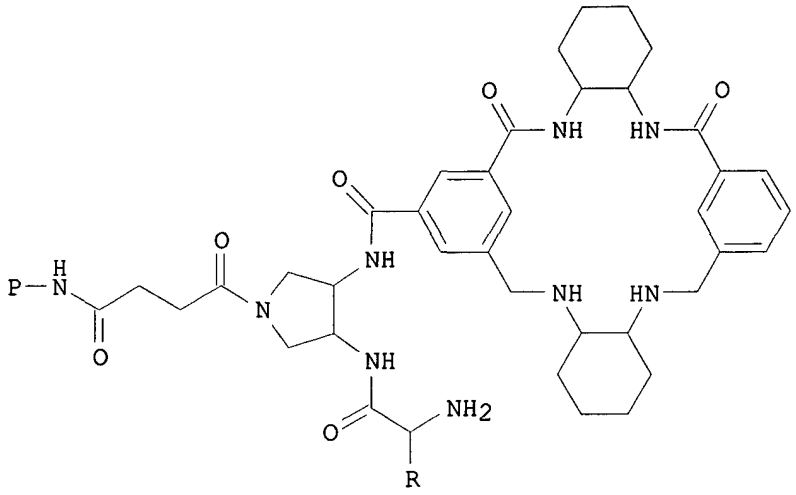
AN 1998:623988 HCAPLUS
DN 129:245494
TI Preparation and screening of betides and **combinatorial libraries**
IN Rivier, Jean E. F.; Porter, John S.
PA The Salk Institute for Biological Studies, USA
SO U.S., 18 pp. Cont.-in-part of U.S. 5,681,928.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE
PI	US 5807986	A	19980915		US 1995-579216	19951228 <--
	US 5681928	A	19971028		US 1994-358184	19941216 <--
	CA 2206258	AA	19960620		CA 1995-2206258	19951215 <--
	US 5807983	A	19980915		US 1996-598424	19960208 <--
PRAI	US 1994-358184		19941216	<--		
	US 1995-579216		19951228	<--		

OS MARPAT 129:245494
AB Compds. termed "betides" mimic **peptides** and contain one or more residues of aminoglycine, C.alpha.-aminoalanine, aminosarcosine, or the like wherein the side chain amino group has been acylated and optionally also alkylated. Generally, betides have the formula: XN-X1-X2-X3-Xm-X4-X5-X6-XC [XN = acyl, other N-terminal group, **peptide** contg. up to about 50 **amino acids**; XC = OH, NH2, other C-terminal group, **peptide** contg. up to about 50 **amino acids**; X1-X6 = independently betidamino acid, .alpha.-**amino acid**, bond; Xm = **peptide** contg. up to about 50 **amino acids**, bond; provided that at least 1 of X1-X6 = betidamino acid residue NRCR0(NR2R3)CO; R0 = H, Me; R, R2 = H, alkyl; R3 = acyl, isocyanate, isothiocyanate, sulfonyl, etc]. To make a betide, an aminoglycine residue is subjected to side chain acylation, and optionally also alkylation, after it is coupled into a **peptide** intermediate. By synthesizing betides with multiple substituents at one or more positions in an otherwise peptidic chain, efficient screening of betides which mimic **peptides** having a large no. of different natural or unnatural **amino acid** substituents at a particular position, and optionally both D- and L-isomers thereof, is possible. Thus, betide Ac-.beta.-D-2-Nal-D-Phe(4-Cl)-DL-Gly(NHCO-4-pyridyl)-Ser-Aph(Ac)-D-Aph(Ac)-Leu-Lys(CHMe2)-Pro-D-Ala-NH2 [Nal = 3-(2-pyridyl)alanine; Aph = 4-aminophenylalanine] was prepd. by solid-phase methods, and the two stereoisomers at the aminoglycine residue sepd. Assaying these two betides in the std. in vivo rat anti-ovulation test shows that, at dosages of 10 .mu.g, 3 out of 7, and 0 out of 8 rats resp. ovulate; at a dosage of 2.5 .mu.g, only the second isomer was bioactive, with 2 out of 8 rats ovulating.
IT **98-88-4**, Benzoyl chloride **122-01-0**, 4-Chlorobenzoyl chloride **874-60-2**
RL: RCT (Reactant)
(prepn. and screening of (acylamino)glycine **peptides** and **combinatorial libraries**)

L94 ANSWER 25 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:532108 HCAPLUS
DN 129:276252
TI Enantioselective Resolving Resins from a **Combinatorial Library**. Kinetic Resolution of Cyclic **Amino Acid** Derivatives
AU Weingarten, M. David; Sekanina, Klara; Still, W. Clark
CS Department of Chemistry, Columbia University, New York, NY, 10027, USA
SO J. Am. Chem. Soc. (**1998**), 120(35), 9112-9113
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English

GI



I

AB A small (60-member) stereoisomeric **combinatorial library** of potential resolving resins I [R = (protected) D- or L-**amino acid** side chain; P = polystyrene support] was prepd. and screened with dye-labeled cyclic **amino acid** derivs. R1-X1-Pro-OC6F5 and R2-X1-L-Pro-OC6F5 (R1 = Disperse Red 1; R2 = Disperse Blue 3; X1 = COCH2CH2CO, m-COC6H4CO). Enantioselective **library** members can be readily distinguished and used in a heterogeneous kinetic resoln. process that corresponds to resoln. by filtration.

IT **99-63-8**, 1,3-Benzenedicarbonyl dichloride
RL: RCT (Reactant)
(kinetic resoln. of cyclic **amino acid** derivs. using enantioselective **combinatorial library** resolving resins)

L94 ANSWER 26 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:474852 HCAPLUS
DN 129:231003
TI Multiple solid-phase synthesis of hydantoins and thiohydantoins
AU Bhalay, Gurdip; Cowell, Daniel; Hone, Neal D.; Scobie, Martin; Baxter, Anthony D.
CS Oxford Diversity, A Division of Oxford Asymmetry Ltd., Oxon, OX14 4RX, UK
SO Mol. Diversity (**1998**), Volume Date 1997-1998, 3(3), 195-198
CODEN: MODIF4; ISSN: 1381-1991
PB Kluwer Academic Publishers
DT Journal
LA English
AB A novel general protocol for the construction of hydantoins and thiohydantoins on a solid support has been developed. Using this novel methodol., the synthesis of a diverse 96-compd. **library** has been achieved. Resin-bound dipeptides are cyclized via the formation of an intermediate isocyanate or isothiocyanate on resin as the key step in the strategy.

IT **503-38-8**, Diphosgene
RL: RCT (Reactant)
(multiple solid-phase synthesis of hydantoins and thiohydantoins)

L94 ANSWER 27 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:424247 HCAPLUS
DN 129:95504
TI **Combinatorial** process for preparing fused pyrimidine

libraries

IN Jagdmann, Gunnar E., Jr.

PA Eli Lilly and Co., USA; Jagdmann, Gunnar E., Jr.

SO PCT Int. Appl., 47 pp.
CODEN: PIXXD2

DT **Patent**

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9827087	A1	19980625	WO 1997-US22839	19971215 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9856983	A1	19980715	AU 1998-56983	19971215 <--
	EP 946549	A1	19991006	EP 1997-953179	19971215 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
PRAI	US 1996-34295		19961218 <--		
	WO 1997-US22839		19971215 <--		

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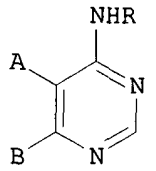

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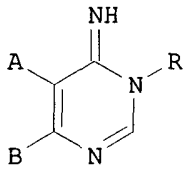

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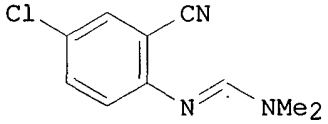
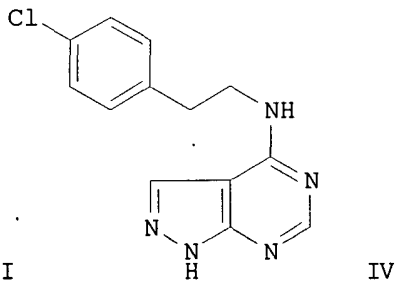


III



IV

AB The invention relates to a novel diverse **combinatorial library** of fused pyrimidine compds., and to an app. providing a readily accessible source of individual members of the **library**. In particular, the **library** is represented by compds. of formulas I or II [AB = atoms to form fused arom. or non-arom. ring; R = org. group derived from an **amine** RNH2]. The app. can be used in assay kits and as a replaceable element in automated assay machines. In one **combinatorial** reaction used to prep. I, arom. formamidines such as III react with primary **amines** in MeCN under heating in 96-well glass titer plates. Exemplary products (4 given) include the pyrazolo[3,4-d]pyrimidine deriv. IV.

IT **403-43-0**, 4-Fluorobenzoyl chloride
RL: RCT (Reactant)
(starting material; prepn. of fused pyrimidine **combinatorial libraries**)

L94 ANSWER 28 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:366719 HCAPLUS
DN 129:136475
TI PEGA supports for **combinatorial peptide** synthesis and solid-phase enzymic **library** assays
AU Renil, Manet; Ferreras, Mercedes; Delaisse, Jean M.; Foged, Niels T.; Meldal, Morten
CS Department of Chemistry, Carlsberg Laboratory, Valby, Den.
SO J. Pept. Sci. (**1998**), 4(3), 195-210
CODEN: JPSIEI; ISSN: 1075-2617
PB John Wiley & Sons Ltd.
DT Journal
LA English
AB Permeable resins cross-linked with long polyethylene glycol (PEG) chains were synthesized for use in solid-phase enzyme **library** assays. High mol. wt. bis-amino-PEG 4000, 6000, 8000 were synthesized by a three-step reaction starting from PEG-bis-OH. Macromonomers were synthesized by partial or diacryloylation of bis-amino-PEG derivs. Bis/mono-acrylamido-PEG were copolymd. along with acrylamide by inverse suspension copolymn. to yield a less cross-linked resin (Type I). Furthermore, acryloyl-sarcosine Et ester was co-polymd. along with bis-acrylamido PEG to obtain more crosslinked capacity resin (Type II). N,N-Dimethylacrylamide was used as a comonomer in some cases. The polymer was usually obtained in a well-defined beaded form and was easy to handle under both wet and dry conditions. The supports showed good mech. properties and were characterized by studying the swelling properties, size distribution of beads, and by estg. the amino group capacity. Depending on the PEG chain length, the monomer compn. and the degree of crosslinking the PEGA supports showed a high degree of swelling in a broad range of solvents, including water, dichloromethane, DMF, MeCN, THF and toluene: no swelling was obsd. in di-Et ether. The PEGA resins (Type I) with an **amino acid** group capacity between 0.07 and 1.0 mmol/g could be obtained by variation of the monomer compn. in the polymn. mixt. Fluorescent quenched **peptide libraries** were synthesized on the new polymer using a multiple column **library** synthesizer and incubated with the matrix metalloproteinase MMP-9 after it had been activated by 4-aminophenyl mercuric acetate resulting in 67/83 kDa active enzyme. The bright beads were sepd. manually under a fluorescence microscope and sequenced to obtain **peptide** substrates for MMP-9. After treatment with ethylenediamine, high-loaded resins (Type II) have been employed in continuous flow **peptide** synthesis to yield **peptides** in excellent yield and purity.
IT **814-68-6**, Acryloyl chloride
RL: RCT (Reactant)
(prepn. of amino-polyethylene glycol supports for **combinatorial peptide** synthesis and solid-phase enzymic **library** assays)

L94 ANSWER 29 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:355631 HCAPLUS
DN 129:136349
TI A solution-phase **combinatorial** parallel synthesis of 3.beta.-amido-3.alpha.-hydroxy-5.alpha.-androstane-17-ones
AU Maltais, Rene; Poirer, Donald
CS Medicinal Chem. Div. LREM, CHUL Res. Cent. Laval Univ., PQ, G1V 4G2, Can.
SO Tetrahedron Lett. (**1998**), 39(24), 4151-4154
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 129:136349
AB A two-level **library** of 3.beta.-amido-3.alpha.-hydroxy-5.alpha.-androstane-17-one compds. was synthesized from a steroid precursor using the soln.-phase parallel synthesis. The compds. were easily obtained in high purity by regioselective aminolysis of the oxirane intermediate

followed by acylation of the **amine**. Since oxiranes can be generated from readily available ketones or alkenes, the proposed strategy give access to a large series of compds.

IT **98-88-4**, Benzoyl chloride **141-75-3**, Butanoyl chloride **142-61-0**, Hexanoyl chloride
RL: RCT (Reactant)
(soln.-phase combinatorial parallel synthesis of 3.beta.-amido-3.alpha.-hydroxy-5.alpha.-androstane-17-ones)

L94 ANSWER 30 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:352856 HCAPLUS
DN 129:41369
TI **Combinatorial** synthesis of **amino acid** -containing thiosaccharides as antibacterial agents
IN Hindsgaul, Ole
PA Synsorb Biotech, Inc., Can.; Hindsgaul, Ole
SO PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 8

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9822487	A1	19980528	WO 1997-CA866	19971114	<--
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	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	US 5780603	A	19980714	US 1996-751231	19961115	<--
	US 6063769	A	20000516	US 1996-751510	19961115	<--
	AU 9850440	A1	19980610	AU 1998-50440	19971114	<--
	EP 938492	A1	19990901	EP 1997-913040	19971114	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
	JP 2001505558	T2	20010424	JP 1998-523031	19971114	<--
PRAI	US 1996-751231	A	19961115	<--		
	US 1996-751510	A	19961115	<--		
	US 1996-30794	P	19961114	<--		
	WO 1997-CA866	W	19971114	<--		

OS MARPAT 129:41369
AB Combinatorial synthesis of **amino acid**-contg. thiosaccharides AYCHR1(CHR3)nCHR2XR4 (A = saccharide; R1-R3 = independently H, alkyl, substituted alkyl, alkenyl, alkaryl, aryl, cycloalkyl, cycloalkenyl, heteroaryl, heterocyclic, thioalkoxyalkyl or joined together to form cycloalkyl, cycloalkenyl, heterocyclic ring; R4 = H, alkyl; X = O, S, SO, SO2, **amide**, acyl; Y = S, SO, SO2; n = 0, 1) optionally attached to a solid support, is reported. Thus, 2-hydroxycyclohex-1-yl 1-thio-.beta.-D-galactopyranoside was prepd. as inhibitor of Heat labile enterotoxin and Cholera toxin binding to ganglioside GD1b by at least 20%.

IT **112-16-3**, Lauroyl chloride
RL: RCT (Reactant)
(prepn. and **combinatorial libraries** of **amino acid**-contg. thiosaccharides)

L94 ANSWER 31 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:331864 HCAPLUS
DN 129:108720
TI Solid phase synthesis of urea **libraries** using a diversifiable thiophenoxy carbonyl linker
AU Dressman, Bruce A.; Singh, Upinder; Kaldor, Stephen W.
CS Lilly Res. Lab., Lilly Corporate Center, Indianapolis, IN, 46285, USA

SO Tetrahedron Lett. (**1998**), 39(22), 3631-3634
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 129:108720
AB A method for the solid phase synthesis of urea **libraries** from primary and secondary **amines** is described which utilizes a thiophenoxy carbonyl linker. Sequential release of different urea products from a common batch of resin using a "milking" procedure has also been accomplished.
IT **7693-46-1**, p-Nitrophenyl chloroformate
RL: RCT (Reactant)
(solid phase synthesis of urea **libraries** using a diversifiable thiophenoxy carbonyl linker)

L94 ANSWER 32 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:251317 HCAPLUS
DN 128:319046
TI Droplet assay system for screening **combinatorial libraries**
IN Schreiber, Stuart L.; Shair, Matthew D.; Borchardt, Allen J.; You, Angie J.; Huang, Jing; Foley, Mike; Tan, Derek; Whitesides, George; Jackman, Rebecca J.
PA President and Fellows of Harvard College, USA
SO PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9816830	A2	19980423	WO 1997-US19110	19971015 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9852391	A1	19980511	AU 1998-52391	19971015 <--

PRAI US 1996-29128 19961016 <--
US 1997-49864 19970606 <--
WO 1997-US19110 19971015 <--

AB The present invention provides a novel system for simultaneously screening a large no. of compds. and identifying compds. having desirable chem. or biol. activities. According to the invention, test compds. are isolated in and introduced into liq. droplets within which their activities are studied. Multiple droplets are displayed simultaneously on a single surface without risk of confusion because the sep. identity of each droplet is maintained and diffusion of test compds. from one droplet to another is avoided. In certain embodiments, these goals are accomplished through reliance on droplet surface tension. In other embodiments, the droplets are localized in micro-wells that retain droplet integrity. The system is particularly useful for identifying compds. that act e.g., as catalysts, or that have biol. activities. In preferred embodiments of the invention, the compds. are assayed in vivo.
IT **103-80-0**, Phenylacetyl chloride
RL: RCT (Reactant)
(droplet assay system for simultaneously assaying **combinatorial libraries** and identifying compds. of **chem.** or biol. activities)

L94 ANSWER 33 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:250009 HCAPLUS

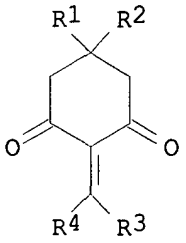
DN 129:4826
TI Solid phase synthesis of benzylamine-derived sulfonamide **library**
AU Kim, Sang Woong; Hong, Chang Yong; Lee, Koo; Lee, Eun Ju; Koh, Jong Sung
CS Biotech Research Institute, LG Chemical Ltd./Research Park, Taejon, 305-380, S. Korea
SO Bioorg. Med. Chem. Lett. (**1998**), 8(7), 735-738
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
AB Using solid phase synthesis, a **library** has been constructed of benzylamine-derived sulfonamides [N-sulfonyl 4-(aminomethyl)phenylalaninamides] which have strong inhibitory activity against the blood coagulant thrombin. The **library** compds. were obtained in good yield and high purity; four of these thrombin inhibitors showed nanomolar potency (Ki 600-10 nM).
IT **7693-46-1**, p-Nitrophenyl chloroformate
RL: RCT (Reactant)
(solid phase synthesis of benzylamine-derived sulfonamide **library**)

L94 ANSWER 34 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:233891 HCAPLUS
DN 128:308380
TI **Combinatorial** synthesis of dihydropyridone **libraries** and their derivatives
AU Creswell, Mark W.; Bolton, Gary L.; Hodges, John C.; Meppen, Malte
CS Parke-Davis Pharmaceutical Research, Division of Warner-Lambert Company, Ann Arbor, MI, 48105, USA
SO Tetrahedron (**1998**), 54(16), 3983-3998
CODEN: TETRAB; ISSN: 0040-4020
PB Elsevier Science Ltd.
DT Journal
LA English
AB Polymer-supported quench methodol. has been used for parallel purifn. of **combinatorial libraries** of dihydropyridones and their derivs. The dihydropyridone scaffold was assembled via a soln.-phase, Lewis-acid-catalyzed hetero-Diels-Alder reaction. Further modifications allow for the rapid generation of subsequent aminopiperidine and (acylamino)piperidine **libraries** utilizing a **library** -from-**library** approach.
IT **98-88-4**, Benzoyl chloride **100-07-2**, Benzoyl chloride, 4-methoxy- **122-01-0**, Benzoyl chloride, 4-chloro- **645-45-4**, Benzenepropanoyl chloride **2719-27-9**, Cyclohexanecarbonyl chloride **5271-67-0**, 2-Thiophenecarbonyl chloride
RL: RCT (Reactant)
(**combinatorial** synthesis of dihydropyridone **libraries** and their derivs.)

L94 ANSWER 35 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:163547 HCAPLUS
DN 128:230629
TI Methods for solid-phase or **combinatorial** synthesis of oligosaccharide
IN Toth, Istvan; Dekany, Gyula; Kellam, Barry
PA Alchemia Pty. Ltd., Australia; Toth, Istvan; Dekany, Gyula; Kellam, Barry
SO PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9808799	A1	19980305	WO 1997-AU544	19970826 <--
	W: AU, CA, CN, HU, JP, US				

RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
AU 9738422 A1 19980319 AU 1997-38422 19970826 <--
AU 728149 B2 20010104
EP 923528 A1 19990623 EP 1997-935368 19970826 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
CN 1234790 A 19991110 CN 1997-199167 19970826 <--
JP 2001501174 T2 20010130 JP 1998-511091 19970826 <--
PRAI AU 1996-1905 A 19960826 <--
WO 1997-AU544 W 19970826 <--
GI



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AB A support for solid-phase or combinatorial synthesis of oligosaccharides, comprising a resin and a 2-substituted-1,3-dioxocycloalkyl linker group I [R1, R2 = same or different H, Me, alky; R3 = amino sugar, glycosylamine, mono- or oligosaccharide coupled through (un)substituted (alkyl, aryl, carboxyalkyl, carboxyaryl, carboxycycloalkyl)amino; R4 = (alkyl, aryl, carboxyalkyl, carboxyaryl, carboxycycloalkyl)amino] was prepd. Thus, (4,4-dimethyl-2,6-(dioxocyclohexylidene)-hexanoic acid-6-yl) 2,3,6-tri-O-benzyl-.beta.-D-galactopyranosyl **amine** (II) was prepd. from a mixt. of 6-hydroxy-6-(4,4-dimethyl-2,6-dioxocyclohexylidene)-hexanoic acid and 2,3,6-tri-O-benzyl-.beta.-D-galactopyranosyl **amine** in abs EtOH under reflux for 2 h.
IT **598-21-0**, Bromoacetyl bromide
RL: RCT (Reactant)
(methods for solid-phase or combinatorial synthesis of oligosaccharide)

L94 ANSWER 36 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:163368 HCAPLUS
DN 128:192221
TI Scavenger assisted **combinatorial** process for preparing **libraries** of **amides**, carbamates, and sulfonamides
IN Kaldor, Stephen Warren; Fritz, James Erwin
PA Eli Lilly and Company, USA
SO Eur. Pat. Appl., 45 pp.
CODEN: EPXXDW
DT **Patent**
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 825164	A2	19980225	EP 1997-304046	19970611 <--
EP 825164	A3	19981028		
R: BE, CH, DE, ES, FR, GB, IT, LI, NL, SE				
CA 2207070	AA	19971214	CA 1997-2207070	19970605 <--
JP 10114685	A2	19980506	JP 1997-158429	19970616 <--
PRAI US 1996-19792		19960614 <--		

AB This invention relates to a novel soln. phase process for the prepn. of **amide**, carbamate, and sulfonamide **combinatorial libraries**. E.g., aminomethylated polystyrene was used to scavenge excess acyl chlorides following the prepn. of **amides** by reaction of acyl chlorides and **amines**.

L94 ANSWER 37 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:131924 HCAPLUS
DN 128:280046
TI Organophosphonate binding Fabs isolated from a human **combinatorial** phage-display **library**
AU Schlager, John J.; Hornyak, Mark J.; Smith, Malcolm M.; Cababa, Douglas; Barbas, Carlos F., III
CS Applied Pharmacology Branch, United States Army Medical Research Institute of Chemical Defense, Aberdeen Proving Ground, MD, 21010-5425, USA
SO Med. Def. Biosci. Rev., Proc. (**1996**), Volume 1, 331-337
Publisher: National Technical Information Service, Springfield, Va.
CODEN: 64UTAN
DT Conference
LA English
AB An expressed human Fab (Fragment:antigen binding) **combinatorial** phage-display **library** cloned into pComb3 was screened and purified using a multistep binding purifn. assay (biopanning) to isolate single phage-expressing Fab that exhibit high affinity binding to a soman analog, methylphosphonate deriv. (MP) {3,3-dimethyl-4-[3-(2-.gamma.-aminolysine)propionyl] amino-S-2-butyl}(methyl)methyl phosphonate (attached to a carrier **protein**). Two stereoisomers of MP, CRPS and CSPS, were used for the screening. Fab **libraries** were constructed by performing oligo-directed mutagenesis within the heavy chain complementary detg. region 3 (CDR3) of a single cloned human tetanus toxoid-specific antibody cloned into the phage-display vector pComb3. The **library** was biopanned for isolation of MP binding phage. Five purified phages obtained from biopanning series against each isomer were singly isolated, grown, and DNA modified for expression of sol. phage. The sequence of the DNA contained in the ten binding phages was performed for **protein** sequence identity. Seven of the ten isolated Fab were detd. to have a different sequence with two sets contg. the same sequence. This produced three different Fab for the CSPS, three Fab for CRPS and one which bound both isomers. The expression and binding characteristics of the Fab to soman acid are presently under investigation.
IT **96-64-0D**, Soman, analogs
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(organophosphonate binding Fabs isolated from a human **combinatorial** phage-display **library**)

L94 ANSWER 38 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:120434 HCAPLUS
DN 128:204634
TI Novel quenchers for solution phase parallel synthesis
AU Nikam, Sham S.; Kornberg, Brian E.; Ault-Justus, Stephanie E.; Rafferty, Michael F.
CS Dep. Chem., Parke-Davis Pharmceutical Div., Warner-Lambert Co., Ann Arbor, MI, 48105, USA
SO Tetrahedron Lett. (**1998**), 39(10), 1121-1124
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 128:204634
AB The bifunctionality of **amino acids** can be exploited by utilizing them as quenchers in rapid soln. phase parallel synthesis. The amino group was used to covalently trap the excess electrophiles, whereas the carboxylic acid moiety was used to solubilize the derivatized **amino acid** in water. As a prototype we used potassium sarcosinate as a quencher for excess electrophiles in the acylation or sulfonation of N-methylbenzylamine. Various electrophilic reagents such as **acid chlorides**, isocyanates and sulfonyl chlorides were quenched successfully to give pure products in excellent yields.
IT **98-88-4**, Benzoyl chloride **103-80-0**, Phenylacetyl chloride **122-04-3**, 4-Nitrobenzoyl chloride **645-45-4**, 3-Phenylpropionyl chloride **2719-27-9**, Cyclohexylcarbonyl

chloride
RL: RCT (Reactant)
(use of potassium sarcosinate as quencher for soln. phase parallel synthesis)

L94 ANSWER 39 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:119787 HCAPLUS
DN 128:192395
TI Arylsulfonate esters in solid phase organic synthesis. II. compatibility with commonly-used reaction conditions
AU Baxter, Ellen W.; Rueter, Jaimie K.; Nortey, Samuel O.; Reitz, Allen B.
CS Drug Discovery Division, R. W. Johnson Pharmaceutical Research Institute, Spring House, PA, 19477, USA
SO Tetrahedron Lett. (**1998**), 39(9), 979-982
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 128:192395
AB The arylsulfonate ester functionality connecting an alkyl chain to a polystyrene resin is compatible with Grignard addns., stabilized Wittig, sodium borohydride redn., reductive aminations, acylations and addn. of various electrophiles, and Suzuki coupling. Cleavage of the resin-bound substrate with **amines** and other nucleophiles can provide diverse compd. **libraries**.
IT **100-07-2**, p-Methoxybenzoyl chloride **122-04-3**, p-Nitrobenzoyl chloride
RL: RCT (Reactant)
(reactions of resin-bound arylsulfonate esters)

L94 ANSWER 40 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:116077 HCAPLUS
DN 128:127607
TI Scavenger assisted **combinatorial** reductive amination process for preparing **libraries** of tertiary **amine** compounds.
IN Hahn, Patric James; Kaldor, Stephen Warren; Siegel, Miles Goodman; Dressman, Bruce Anthony; Fritz, James Erwin
PA Eli Lilly and Co., USA
SO Eur. Pat. Appl., 37 pp.
CODEN: EPXXDW
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 816310	A2	19980107	EP 1997-304049	19970611 <--
	EP 816310	A3	19990224		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	CA 2207088	AA	19971214	CA 1997-2207088	19970605 <--
	JP 10120631	A2	19980512	JP 1997-158563	19970616 <--
PRAI	US 1996-19790		19960614 <--		

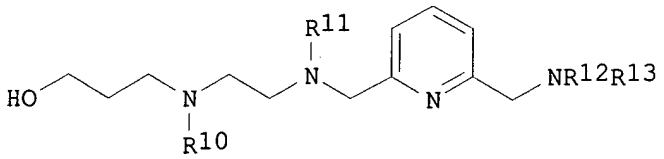
AB **Combinatorial libraries** of R1R2NCH2R3 (R1-R3 = noninterfering substituents) were prepd. by reaction of R3CHO with .gtoreq.1.1 equiv. R1R2NH in sep. reaction zones in the presence of reducing agents followed by addn. of solid supported **amine** reactive scavengers. Various 1-substituted piperazines and arom. aldehydes reacted in the presence of cyanoborohydride resin followed by addn. of **acid chloride** resin to give the corresponding 1,4-disubstituted piperazines.

L94 ANSWER 41 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:112497 HCAPLUS
DN 128:180338
TI Preparation of compounds or **combinatorial libraries** of compounds having a plurality of nitrogenous substituents

IN Cook, P. Dan; An, Haoyun
PA ISIS Pharmaceuticals, Inc., USA; Cook, P. Dan; An, Haoyun
SO PCT Int. Appl., 187 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9805961	A1	19980212	WO 1997-US13530	19970801 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 6077954	A	20000620	US 1996-691206	19960801 <--
	AU 9739036	A1	19980225	AU 1997-39036	19970801 <--
	US 6197965	B1	20010306	US 1999-312988	19990517 <--
PRAI	US 1996-691206	A2	19960801 <--		
	WO 1997-US13530	W	19970801 <--		

OS MARPAT 128:180338
GI



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AB Novel compds. of general formula L-T-[-N(T-L)(CH2)x-]r-A[(J)t-T-L]-[-(CH2)x-N(T-L)]s-T-L [r = 1-4; s = 2-4; A = arom., heterocyclic, alicyclic ring; x = 1-8; J = N, O, S, heterocyclic ring system having at least one N; t = 0,1; T = single bond, CH2, [(CR1R2)m-R5-(CR1CR2)n-[C(:R6)]p-E]q; R1, R2 = H, C1-10 alkyl or haloalkyl, C2-10 alkenyl or alkynyl, C6-14 aryl; R5, E = single bond, CH:CH, C.tplbond.C, O, S, (un)substituted NH, SO2, (un)substituted C6-14 aryl, (un)substituted heteroaryl, (un)substituted (mixed) heterocycle contg. a N, O, or S; R6 = O, S, (un)substituted NH; m, n = 0-5; p = 0,1; q = 1-10; L = H, (un)substituted C1-10 alkyl, C2-10 alkenyl, or C4-7 carbocyclic alkyl, (un)substituted alkyl, alkenyl, or alkynyl carbocyclic, (un)substituted C6-14 aryl or heteroaryl, (un)substituted heterocycle contg. a N, O, or S, (un)substituted (mixed) heterocycle; with proviso that when A = 2,6-disubstituted pyridine with r = s = 2 and 6 of said L groups, then not more than 3 of said L groups are H or p-toluenesulfonyl] are constructed to include a central arom., aliph., or heterocyclic ring system. Attached to the central ring system are two linear groups having nitrogenous moieties that are derivatized with chem. functional groups. The ring system can include further nitrogenous moieties, either as ring atoms or on pendant groups attached to the ring, that may also be derivatized with chem. functional groups. The totality of the chem. functional groups imparts certain conformational and other properties to these compds. In accordance with certain embodiments of the invention, **libraries** of such compds. are prepd. utilizing permutations and combinations of the chem. functional groups and the nitrogenous moieties to build complexity into the **libraries**. Such **libraries** are useful as antibacterial, antifungal, and imaging agents or for identifying metal chelating species for heavy metal therapy as well as industrial application. Thus, 2-(acetamidomethyl)pyridine deriv. (I; R10 = Boc, R11 = R12 = H, R13 = CH2CONH2) (prepn. given) was alkylated by

3-(trifluoromethyl)benzyl bromide in the presence of K2CO3 in MeCN followed by treatment with CF3CO2H in CHCl3 at room temp. for 4 h to give I (R10 = H, R11 = R12 = 3-(trifluoromethyl)benzyl, R13 = CH2CONH2), which in vitro at 100 .mu.M inhibited 95% Staphylococcus pyogenes and 87% Escherichia coli. Many **libraries** of compds. were also prepd., e.g., by alkylating I (R10 = Boc, R11 = R12 = R13 = H) with a mixt. of benzyl bromide, 3-fluorobenzyl bromide, .alpha.-bromo-m-xylene, Me 3-bromomethylbenzoate, 3-nitrobenzyl bromide, and 3-(trifluoromethyl)benzyl bromide in MeCN at room temp. overnight followed by deprotection with CF3CO2H to give a **library** of compds. N-benzylated (hydroxydiazaoctyl)(aminomethyl)pyridine I [R10 = H; R11, R12, R13 are randomly selected from benzyl, 3-fluorobenzyl, 3-methylbenzyl, 3-(methoxycarbonyl)benzyl, 3-nitrobenzyl] having m/z 663-867 in mass spectroscopy, which showed min. inhibitory concn. of 1-5, 1-5, 1-5, and 5-25 .mu.g/mL against Staphylococcus aureus, Staphylococcus pyogenes, Escherichia coli, and Candida albicans, resp., and inhibited 68% phospholipase A2 and 31% tat/TAR RNA/**protein** interactions at 100 .mu.M, and.

IT **75-36-5**, Acetyl chloride **98-88-4**, Benzoyl chloride **598-21-0**, Bromoacetyl bromide
RL: RCT (Reactant)
(prepn. of compds. or **combinatorial libraries** of compds. having plurality of nitrogenous substituents as drugs such as antibacterial and antifungal agents)

L94 ANSWER 42 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:79418 HCAPLUS
DN 128:166998
TI System for multiple simultaneous synthesis of small-molecule organic compounds
IN Dewitt, Sheila H. H.; Kiely, John S.; Pavia, Michael R.; Schroeder, Mel C.; Stankovic, Charles J.
PA Warner-Lambert Co., USA
SO U.S., 67 pp. Cont.-in-part of U.S. Ser.5,612,002.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	US 5714127	A	19980203		US 1995-475559	19950607	<--
	US 5324483	A	19940628		US 1993-12557	19930202	<--
	US 5324483	B1	19960924				
	US 5612002	A	19970318		US 1995-430696	19950428	<--
	US 5565173	A	19961015		US 1995-461998	19950605	<--
	US 5567391	A	19961022		US 1995-464161	19950605	<--
	US 5582801	A	19961210		US 1995-463545	19950605	<--
	US 5593642	A	19970114		US 1995-461475	19950605	<--
	US 5766556	A	19980616		US 1996-777270	19961231	<--
PRAI	US 1992-958383		19921008	<--			
	US 1993-12557		19930202	<--			
	US 1994-217347		19940324	<--			
	US 1995-430696		19950428	<--			

AB A system for the multiple, simultaneous synthesis of org. compds., primarily by the solid-phase method, is disclosed. The system includes: (a) a sealed reaction app. comprising a reservoir member with a plurality of reaction wells for holding reaction materials, a plurality of tubular members (usually gas dispersion tubes) for holding reaction materials, a holder member attached to the reservoir for holding the tubular members, and a manifold member attached to the holder member and enclosing a portion of the tubular members, (b) a sample processor, (c) a means on the sample processor for dispensing and aspirating materials at least into and from said tubular members, (d) a first controller for the operation of the sample processor, including the dispensing and aspirating of materials into and from the tubular members, (e) a multi-axis robot member for manipulating the reaction app. on the sample processor, and (f) a second

controller, for operation of the multi-axis robot member, in order to manipulate the reaction app. on the sample processor. The manifold top wall has a plurality of apertures in axial alignment with the reaction tubes, and a gasket which allows penetration by a needle in order to dispense and aspirate materials from the reaction tubes. Sealing members, such as gaskets, are placed between the holder block, manifold, and reservoir rack, and the components are releasably fastened together. A robotic sample processor is used to automate the synthesis process using the reaction app. The app. is constructed from materials which will accommodate heating, cooling, agitation, or corrosive reagents. The app. provides in excess of 1 mg of each product with structural knowledge and control over each compd. The app. can be adapted to manual, semiautomatic, or fully automatic performance. Using the app., a series of building blocks are covalently attached to a solid support. These building blocks are then modified by covalently adding addnl. different building blocks or chem. modifying some existing functionality until the penultimate structure is achieved. This is then cleaved from the solid support by another chem. reaction into the soln. within the well, yielding an array of newly synthesized individual compds., which after post-reaction modification, if necessary, are suitable for testing for activity. A variety of org. compds. with different functionalities may be prepd. by the system, including **peptides**, cyclic **peptides**, hydantoins, benzodiazepines, keto-ureas, nucleosides or analogs, cyclic nucleotides, carbocyclic compds. (e.g. tocopherols and steroids) and other N-, O-, and S-contg. heterocyclic compds. (e.g., .beta.-lactams and cephalosporins). The system is suitable for synthesizing compds. in an array format based on a structure of known biol. activity, for the purpose of developing a structure activity relationship for biol. agents such as muscarinic agonists, antiepileptics, antidepressants, HMG CoA reductase inhibitors, antiinflammatories, etc. Among several groups of compds. prepd. in examples, 16 dipeptides contg. Ala or Ile were prepd. in 26-85% yield, 40 hydantoins were prepd. in 5-81% yield, and 40 benzodiazepines were prepd. <5% to quant. yield.

IT **98-88-4**, Benzoyl chloride **121-90-4**, 3-Nitrobenzoyl chloride
RL: RCT (Reactant)
(acylation; system for multiple simultaneous synthesis of small-mol. org. compds.)

IT **10400-19-8**, Nicotinoyl chloride
RL: RCT (Reactant)
(condensation reaction; system for multiple simultaneous synthesis of small-mol. org. compds.)

IT **75-36-5**, Acetyl chloride **100-07-2**, p-Anisoyl chloride **122-01-0**, 4-Chlorobenzoyl chloride **122-04-3**, 4-Nitrobenzoyl chloride **3282-30-2**, Pivaloyl chloride
RL: RCT (Reactant)
(esterification; system for multiple simultaneous synthesis of small-mol. org. compds.)

L94 ANSWER 43 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:71280 HCAPLUS
DN 128:141020
TI Preparation of quinoline derivatives and quinoline **combinatorial libraries**
IN Pei, Yazhong; Kiely, John S.
PA Trega Biosciences, Inc., USA
SO PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9802741	A1	19980122	WO 1997-US11888	19970710 <--

W: AU, CA, JP
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

	US 5840500	A	19981124	US 1996-678136	19960711 <--
	CA 2260177	AA	19980122	CA 1997-2260177	19970710 <--
	AU 9735975	A1	19980209	AU 1997-35975	19970710 <--
	EP 923734	A1	19990623	EP 1997-932543	19970710 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, IE				
	JP 2000516208	T2	20001205	JP 1998-506108	19970710 <--
	US 6143895	A	20001107	US 1998-137501	19980820 <--
PRAI	US 1996-678136	A	19960711 <--		
	WO 1997-US11888	W	19970710 <--		

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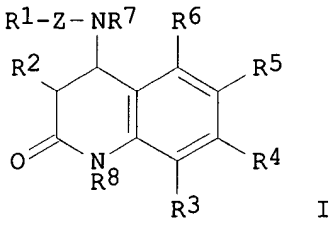


I

AB Tetrahydroquinolines I [Z = (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, Ph, naphthyl, phenylalkyl, alkylenearylenealkylene; R1 = CO2H, OH, SH, amino, carboxamido, CH2OH, CH2NH2, aminomethyl; R2 = OH, (un)substituted alkoxy, acyloxy, amino, etc.; R3-R6 = H, halo, OH, cyano, nitro, alkyl, etc.; R7, R8 = H, (un)substituted alkyl, acyl, phenylsulfonyl, etc.] and **combinatorial libraries** composed of such compds. were prepd. Thus, a **combinatorial library** of tetrahydroquinolines, including 4-[N-(1-carboxyethyl)amino]-3,4-dihydro-3-(4-chlorophenoxy)-2(1H)-quinolinone, was prepd. via condensation of 2-nitrobenzaldehyde, 4-chlorophenoxyacetyl chloride, and various **amino acids** on a polystyrene Wang resin. Compds. within a synthetic **combinatorial library** mixt. were assayed for binding to the .kappa. opioid receptor.

IT **701-99-5**, Phenoxyacetyl chloride **38870-89-2**, Methoxyacetyl chloride
RL: RCT (Reactant)
(prepn. of (carboxyalkylamino)quinolines and quinoline **combinatorial libraries**)

L94 ANSWER 44 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:71151 HCAPLUS
DN 128:176155
TI Conjugates of soluble peptidic compounds with membrane-binding agents for treatment of inflammation and thrombotic disorders
IN Smith, Richard Anthony Godwin; Dodd, Ian; Mossakowska, Danuta Ewa Irena
PA Adprotech PLC, UK; Smith, Richard Anthony Godwin; Dodd, Ian; Mossakowska, Danuta Ewa Irena
SO PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9802454	A2	19980122	WO 1997-EP3715	19970708 <--
	WO 9802454	A3	19980402		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,				

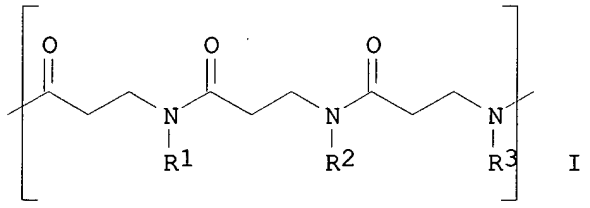
GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9736939	A1	19980209	AU 1997-36939	19970708	<--
EP 912730	A2	19990506	EP 1997-933665	19970708	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2000515370	T2	20001121	JP 1998-505608	19970708	<--
ZA 9706216	A	19990414	ZA 1997-6216	19970714	<--
PRAI GB 1996-14871	A	19960715	<--		
WO 1997-EP3715	W	19970708	<--		

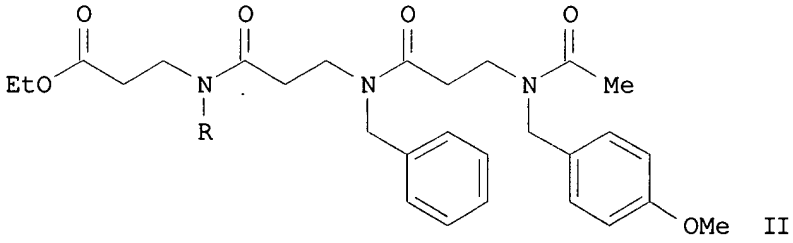
AB Sol. derivs. of sol. **polypeptides** incorporating membrane-binding elements, their use in therapy and methods and intermediates including **peptide** membrane-binding elements are disclosed which can be used in treatment of inflammation and thrombotic disorders.

IT **112-64-1**, Myristoyl chloride
RL: RCT (Reactant)
(conjugates of sol. peptidic compds. with membrane-binding agents for treatment of inflammation and thrombotic disorders)

L94 ANSWER 45 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:45464 HCAPLUS
DN 128:128268
TI Solid Phase Synthesis of .beta.-Peptoids: N-Substituted .beta.-Aminopropionic Acid Oligomers
AU Hamper, Bruce C.; Kolodziej, Stephen A.; Scates, Angela M.; Smith, Ronald G.; Cortez, Enriqueta
CS Monsanto Company, St. Louis, MO, 63167, USA
SO J. Org. Chem. (**1998**), 63(3), 708-718
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
GI



I



II

AB A solid-phase org. synthesis method has been developed for the prepn. of N-substituted-.beta.-aminopropionic acid oligomers or .beta.-peptoids I. Treatment of polymer-bound 4-(benzyloxy)benzyl acrylate with primary **amines** afforded N-substituted .beta.-alanines. Polymer loadings and product conversions were detd. by direct cleavage of resin-bound materials and measurement by 1H NMR with an internal std. The NMR method was used to establish loading of all resin-bound intermediates including acrylic acid. Acylation with acryloyl chloride followed by Michael addn. of primary **amines** to the acrylamide allowed prepn. of di-.beta.-peptoids. By a linear set of seven reactions, trimeric N-benzyl-.beta.-aminopropionic acid was prepd. in 67% overall yield.

Single-bead FT-IR microspectroscopy was used to acquire spectra of the resin bound mono-.beta.-peptoids, di-.beta.-peptoids, and acrylamide intermediates. A **combinatorial library** of defined mixts. of tri-.beta.-peptoids was prepd. by mixing equimolar amts. of the mono-.beta.-peptoid resins and carrying them through two sequences of the acylation-Michael addn. The identity of a sample mixt. II (R = Me, CH2Ph, CH2CH2Ph, CH2C6H4OMe-4, allyl, CH2CHMe2, CHMeEt, CHMe2) was detd. by LC-MS anal. of the cleavage product.

IT **814-68-6**, Acryloyl chloride
RL: RCT (Reactant)
(solid-phase synthesis of substituted aminopropionic acid oligomers)

L94 ANSWER 46 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:684368 HCAPLUS
DN 127:331750
TI Mass-based encoding and qualitative analysis of **combinatorial libraries**
IN Geysen, Hendrik Mario; Kinder, Daniel Start; Wagner, Craig Daniel
PA Glaxo Group Ltd., UK; Geysen, Hendrik Mario; Kinder, Daniel Start; Wagner, Craig Daniel
SO PCT Int. Appl., 404 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9737953	A1	19971016	WO 1997-US5701	19970408 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2242171	AA	19971016	CA 1997-2242171	19970408 <--
AU 9727237	A1	19971029	AU 1997-27237	19970408 <--
EP 863858	A1	19980916	EP 1997-921109	19970408 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRAI US 1996-14970 19960408 <--
WO 1997-US5701 19970408 <--

AB The insertion of isotopically labeled portions into solid state **combinatorial** synthesis constructs followed by mass spectrometric, mass-based NMR spectrometric, or mass-based IR spectrometric anal. allows for the phys., non-**chem**. encoding of large nos. of **combinatorial** synthesis products. Isotopically labeled **peptides** for mass spectral anal. were synthesized for use in four encoding approaches.

IT **28920-43-6**
RL: RCT (Reactant)
(mass-based encoding and qual. anal. of **combinatorial libraries**)

L94 ANSWER 47 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:640838 HCAPLUS
DN 127:307680
TI Methods for spatially-dispersed positionally-encoded **combinatorial library** synthesis
IN Moran, Edmund J.; Cargill, John F.; Maiefski, Romaine R.; Baiga, Thomas J.
PA Ontogen Corp., USA
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT **Patent**
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9735198	A1	19970925	WO 1997-US4500	19970321 <--
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2249419	AA	19970925	CA 1997-2249419	19970321 <--
	AU 9725373	A1	19971010	AU 1997-25373	19970321 <--
	EP 904540	A1	19990331	EP 1997-916869	19970321 <--
	R: DE, FR, GB				
PRAI	US 1996-13897		19960322 <--		
	WO 1997-US4500		19970321 <--		

AB The present invention relates to a method useful in **combinatorial chem.** More specifically, the present invention relates to methods for synthesizing spatially-dispersed positionally-encoded **combinatorial chem. libraries** of oligomers whereby the synthesis is carried out on a plurality of solid supports which in turn are distributed in the form of a series of arrays. The position of each solid support in each array dets. the exact identity of the oligomer.

IT **75-36-5**, Acetyl chloride **79-03-8**, Propionyl chloride **98-88-4**, Benzoyl chloride **103-80-0**, Phenylacetyl chloride **142-61-0**, Hexanoyl chloride **527-69-5**, 2-Furoyl chloride **609-65-4**, 2-Chlorobenzoyl chloride **2719-27-9**, Cyclohexanecarbonyl chloride **4023-34-1**, Cyclopropanecarbonyl chloride **5271-67-0**, 2-Thiophenecarbonyl chloride **21615-34-9**, 2-Methoxybenzoyl chloride
RL: RCT (Reactant)
(methods for spatially-dispersed positionally-encoded **combinatorial library** synthesis)

L94 ANSWER 48 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:533655 HCAPLUS
DN 127:220799
TI Preparation of non-nucleotide phosphorus ester oligomers and their **combinatorial libraries** as selective target-binding compounds
IN Gentles, Robert G.; Cook, Alan F.; Rudolph, Morris J.; Fathi, Reza
PA Pharmagenics, Inc., USA
SO PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DT **Patent**
LA English

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9728168	A1	19970807	WO 1997-US1060	19970122 <--
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 6008398	A	19991228	US 1996-595264	19960201 <--
	AU 9717532	A1	19970822	AU 1997-17532	19970122 <--
	EP 880532	A1	19981202	EP 1997-933585	19970122 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2000506513	T2	20000530	JP 1997-527718	19970122 <--
PRAI	US 1996-595264		19960201 <--		
	US 1995-374040		19950118 <--		
	WO 1997-US1060		19970122 <--		

AB A P ester oligomer is claimed having the monomeric units B1R1[OP(O)(A)OR1]nB2 [A = same or different in each monomeric unit, independently selected from O, S, lower alkyl, (un)substituted alkylamino, (un)substituted arylamino and aminoalkyl; B1 and B2 = same or different, independently selected from H, lower alkyl, a labeling group, a protecting group, a phosphoramidate or a phospho-monoester; R1 can be the same or different in each monomeric unit, and in at least one of the non-nucleotide monomeric units, R1 is independently selected from a

condensation product of (i) a non-vicinal diol attached to an H-bond donor functionality; (ii) an H-bond acceptor selected from an ether, a purine or pyrimidine substituted 1,2-diol or a disubstituted heterocycle; (iii) a non-vicinal diol attached to a hydrophobic functionality or a vicinal diol attached to an aliph. or alicyclic hydrophobic functionality; (iv) a diol attached to a ring substituted anionic functionality and (v) a cationic moiety attached to a non-vicinal or alicyclic diol, any of which can further include a detectable label; n .gtoreq. 1]. Preferred R1 moieties include condensation products of heterocyclic diols, alicyclic diols, and polycyclic diols. The non-nucleotide monomers thereof, **combinatorial library** mixts. of the oligomers and the use of the oligomers as selective target-binding compds. are claimed. In an example, when a **library** of non-nucleotide phosphorus ester oligomers is screened against thrombin, a subpopulation (0.001-0.01%) of the original **library** binds to the target, with an apparent Kd < 100-500 nM.

IT **89992-70-1**
RL: RCT (Reactant)
(prepn. of non-nucleotide phosphorus ester oligomers)

L94 ANSWER 49 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:278944 HCAPLUS
DN **126:251413**
TI Method for controlling mass redundancies in synthetic **combinatorial libraries**
IN Hughes, Ian
PA Smithkline Beecham Plc, UK; Hughes, Ian
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9708190	A2	19970306	WO 1996-EP3731	19960823 <--
	WO 9708190	A3	19970327		
	W: JP, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 852583	A2	19980715	EP 1996-930092	19960823 <--
	R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
	JP 11513027	T2	19991109	JP 1996-509838	19960823 <--
PRAI	GB 1995-17661		19950830 <--		
	WO 1996-EP3731		19960823 <--		

AB The invention provides a method for the control of mass redundancies in a **combinatorial** synthesized compd. **library** which composes identifying compds. by their mol. wt. The invention is based on the principle that each compd. in the **library** will have, by design, a unique mol. wt. which can serve as an identifier for that particular compd. The advantages of this method over tagging synthesis beads are: 1) this invention does not impose any restrictions on the nature of the **chem**. used to synthesize the **combinatorial library**, 2) this invention does not involve addnl., non-synthetically productive tagging steps, and 3) the ability to identify the compd. by its nominal mass without recourse to high resoln. mass spectrometry. Thus, alkylation of polymer-bound triphenylphosphine with 3-BrCH2C6H4CH2N(Boc)2, followed by acidic deprotection, coupling with protected **amino acids** Fmoc-NH-Z-CO2H [Z = CH2, CH2CH2, (CH2)5, p-CH2C6H4; Fmoc-NH-Z-CO2H = 4-(9-fluorenylmethoxycarbonylaminomethyl)cyclohexanecarboxylic acid] further deprotection, acylation with **acid chlorides** RCOCl [R = Pr, 2-furyl, PhCH2, PhCH:CH, MeO2C(CH2)4, 1-naphthyl, H2C:CH(CH2)8, 2,5-(MeO)2C6H3CH2, 4-F-3-CF3C6H3, 4-Me(CH2)6C6H4], and resin cleavage gave 50-member **combinatorial library** 3-MeC6H4CH2NHCO-Z-NHCOR, all with unique mol. wts.

IT **79-03-8**, Propionyl chloride **98-88-4**, Benzoyl chloride **102-92-1**, Cinnamoyl chloride **103-80-0**, Phenylacetyl chloride **122-04-3**, 4-Nitrobenzoyl chloride **141-75-3**,

Butyryl chloride **527-69-5**, 2-Furoyl chloride **874-60-2**, p-Toluoyl chloride **2094-72-6**, 1-Adamantanecarbonyl chloride **2719-27-9**, Cyclohexanecarbonyl chloride **10400-19-8**, Nicotinoyl chloride
RL: RCT (Reactant)
(method for controlling mass redundancies in synthetic **combinatorial libraries**)

L94 ANSWER 50 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:233953 HCAPLUS
DN 126:330414
TI **Combinatorial** synthesis of C(2),C(3)-disubstituted 3-hydroxypropionamides utilizing Baylis-Hillman reactions on solid support
AU Prien, O.; Rolfing, K.; Thiel, M.; Kunzer, H.
CS Research Laboratories, Schering A.-G., Berlin, D-13342, Germany
SO Synlett (**1997**), (3), 325-326
CODEN: SYNLES; ISSN: 0936-5214
PB Thieme
DT Journal
LA English
OS CASREACT 126:330414
AB A 4-step reaction protocol for multiple polymer-supported synthesis of structurally diverse .alpha.,.beta.-disubstituted 3-hydroxypropionamides was developed. Variable building blocks were primary/secondary **amines** and aryl aldehydes, the latter of which underwent incorporation into target mols. via Baylis-Hillman reactions. The machine-assisted assemblage of a small prototype **library** is described.
IT **814-68-6**, Acryloyl chloride
RL: RCT (Reactant)
(combinatorial synthesis of hydroxypropionamides via Baylis-Hillman reaction on solid support)

L94 ANSWER 51 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:218627 HCAPLUS
DN 126:277102
TI Model Studies for New o-Nitrobenzyl Photolabile Linkers: Substituent Effects on the Rates of Photochemical Cleavage
AU Holmes, Christopher P.
CS Affymax Research Institute, Palo Alto, CA, 94304, USA
SO J. Org. Chem. (**1997**), 62(8), 2370-2380
CODEN: JOCEAH; ISSN: 0022-3263
PB American Chemical Society
DT Journal
LA English
OS CASREACT 126:277102
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Both a model phenacyl and o-nitrobenzyl photolabile linker from the literature along with four new o-nitrobenzyl linkers were prepd. and the kinetics of their photolytic cleavage examd. in soln. The linkers were prepd. by amidation of the carboxylic acid anchoring tether with benzylamine, and the cleavable benzylic substituent was chosen to be either acetic acid or acetamide. Irradn. of the linkers in four solvents [methanol, p-dioxane, and aq. buffer (.+-.)-dithiothreitol] at 365 nm and anal. via HPLC afforded kinetic rates of cleavage suitable for comparative purposes. The phenacyl linker was found to cleave slowly under aq. conditions with no detectable cleavage being obsd. in the org. solvents. Known o-nitrobenzyl linker I showed modest rates of cleavage in aq. and org. solvents. Incorporation of two alkoxy groups in the benzene ring to generate the veratryl-based linker II increased the rate of cleavage

dramatically, and introduction of an addnl. benzylic Me group (III) increased the rate of cleavage by roughly 5 fold. Increasing the length of the anchoring carboxylic acid tether from acetic to butyric acid (IV) improved the cleavage kinetics modestly in org. media and slightly diminished the rates in water. The **amide** linker V cleaved from 3 to 7 times faster than the corresponding ester linkage IV. An **amide**-generating linker VI was prepd., and its performance to generate photolabile solid supports was briefly examd. The stability of the linker and subsequent cleavage upon photolysis from the support of an isotopically enriched 4-thiazolidinone was demonstrated by gel phase 13C NMR.

IT **28920-43-6**
RL: RCT (Reactant)
(models for o-nitrobenzyl photolabile linkers and substituent effects on rates of photochem. cleavage)

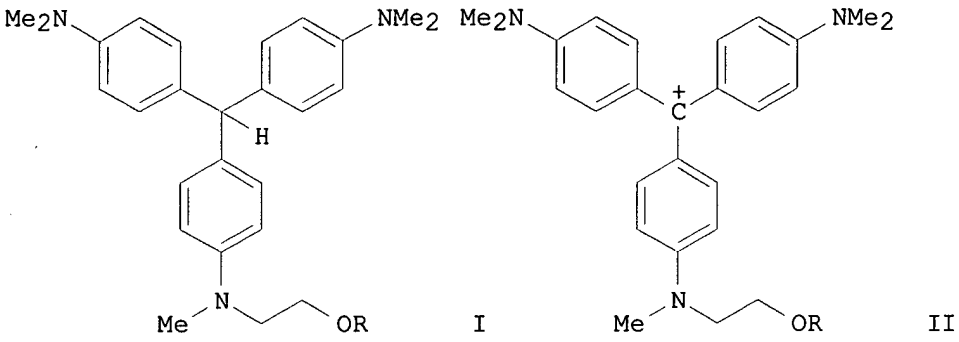
L94 ANSWER 52 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:218113 HCAPLUS
DN 127:44164
TI Direct identification by IR microscopy
AU Deusen, Christoph
CS Germany
SO LaborPraxis (**1997**), 21(3), 32
CODEN: LAPRDE; ISSN: 0344-1733
PB Vogel
DT Journal
LA German
AB Reaction products bond on polymer beads (**combinatorial chem.**) are directly identified by IR-microscopy. The reaction of a bead-bonded **amine** at beads of polystyrene core and poly(ethylene glycol) shell was exemplified. The bead-bonded **amine** was reacted with acetanhydride (I) or with trichloroethyl chloroformate (II). The reaction-product with I showed IR absorption bands of an **amide** and addnl. Me-groups whereas the reaction-product with II had bands deriving from an ester and a CNH-group.
IT **17341-93-4D**, reaction product with amino modified polyethyleneglycol
RL: AMX (Analytical matrix); FMU (Formation, unclassified); ANST (Analytical study); FORM (Formation, nonpreparative)
(direct identification of solid-phase reaction products by IR microscopy)

L94 ANSWER 53 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:169127 HCAPLUS
DN 126:250787
TI Reversible charge-based sequestration on solid support and application to organic synthesis
IN Zepp, Charles M.
PA Versicor, Inc., USA
SO U.S., 19 pp.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5605616	A	19970225	US 1995-553842	19951106 <--
WO 9717310	A1	19970515	WO 1996-US17725	19961105 <--

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9676075 A1 19970529 AU 1996-76075 19961105 <--
PRAI US 1995-553842 19951106 <--
WO 1996-US17725 19961105 <--
OS CASREACT 126:250787
GI



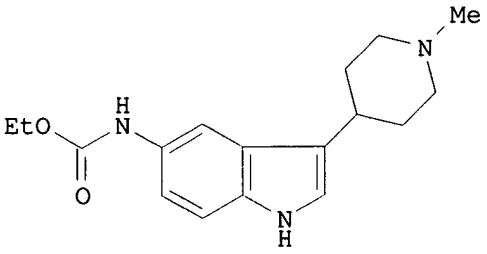
AB Methods for reversibly assocg. a substrate compd. and a solid support are described. In general, the methods feature the use of selectively chargeable moieties, such as dye structures, as linkers which can reversibly bind to a solid support. The solid support may also be selectively chargeable. App. of the invention methods, for example in **high-throughput**, solid-phase synthesis and screening of drug candidates, is also described. For instance, the leuco form crystal violet deriv. I [R = H] was esterified with ClCOCH2Cl, and the resultant I [R = COCH2Cl] was oxidized with o-chloranil to the cationic dye II [R = COCH2Cl]. The latter was readily bound to Florisil, which was then isolated by filtration and washed. The purified, Florisil-bound I was then reduced with NaBH3CN to give back a soln. of the leuco form I [R = COCH2Cl], which was then thio-etherified with PhSH and LiN(SiMe3)2 to give I [R = COCH2SPh]. This was oxidized with DDQ in THF to give II [R = COCH2SPh], which was bound to Florisil, then purified by filtration and washing. Finally, cleavage of the product from both the linker and support using HCl in MeOH-MeOAc mixt. gave a 36.6% combined yield of PhSCH2CO2H and PhSCH2CO2Me in a ratio of 2.83:1.08.
IT **79-04-9**, Chloroacetyl chloride
RL: RCT (Reactant)
(starting material; prepn. of org. compds. via reversible charge-based sequestration of dye linkers on solid support)

L94 ANSWER 54 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:145241 HCAPLUS
DN 126:157395
TI Process for parallel synthesis of a non-**peptide library**
IN Fritz, James E.; Kaldor, Stephen W.
PA Lilly, Eli, and Co., USA; Fritz, James E.; Kaldor, Stephen W.
SO PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9700244	A1	19970103	WO 1996-US10454	19960617 <--

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,

IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM
AU 9663861 A1 19970115 AU 1996-63861 19960617 <--
PRAI US 1995-310 P 19950619 <--
US 1995-492277 A2 19950619 <--
WO 1996-US10454 W 19960617 <--
OS CASREACT 126:157395; MARPAT 126:157395
GI



II

AB A process for the sequential prepn. of a **library** of compds. having pharmaceutical usage is claimed. The process is specifically applicable to indole derivs. R2N(A)XR1 [I; wherein A = indole analog; X = bond, CO, CS; R1 = H, alkyl, aryl, cycloalkyl, heterocyclyl, NR3R4, or OR5; R2, R3, R4 = H, alkyl, aryl, cycloalkyl, heterocyclyl, or their substituted analogs; R1 .noteq. R2 when X = bond; R5 = H, alkyl, aryl, cycloalkyl, or their substituted analogs]. The process involves the sequential mixing of soln. phase reagents, followed by scavenging of excess unreacted reagents with solid phase scavenging agents. The process is highly iterative and applicable to prodn. of various ureas, thioureas, **amides**, carbonates and tertiary **amines**. For example, 5-amino-3-(1-methylpiperidin-4-yl)-1H-indole reacted with ClCOEt in CH2Cl2 in the presence of polyvinylpyridine at room temp. for 2 days. The mixt. was treated with aminomethylated polystyrene for 18 h and evapd. to give 84% title compd. II. Over 50 compds. I were prepd. In selectivity tests against 4 serotonin receptor subtypes, II had a Ki value of 2.8 nM at 5-HT1F receptors, vs. 6.1 nM at 5-HT1A, 38.3 nM at 5-HT1D.alpha., and 182.8 nM at 5-HT1D.beta. receptors. A study of sumatriptan succinate and 4 other compds. at 4 receptor subtypes is also described, with the binding at 5-HT1F receptors showing a 0.94 correlation factor to inhibition of **protein** extravasation.

IT **79-44-7**, Dimethylcarbamoyl chloride **88-10-8**, Diethylcarbamoyl chloride **933-88-0**, 2-Methylbenzoyl chloride **1490-25-1**, 3-(Methoxycarbonyl)propanoyl chloride **1885-14-9**, Phenyl chloroformate **38870-89-2**, Methoxyacetyl chloride
RL: RCT (Reactant)
(starting material; parallel synthesis of indole deriv. **library** as 5-HT1F agonists)

L94 ANSWER 55 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:127453 HCAPLUS
DN 126:144106
TI **Combinatorial libraries** having aminodiol monomer subunits
IN Hebert, Normandy
PA Isis Pharmaceuticals, Inc., USA; Hebert, Normandy
SO PCT Int. Appl., 174 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 4

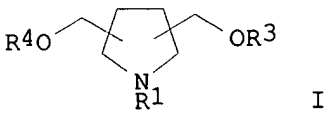
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9640672	A1	19961219	WO 1996-US9604	19960607 <--

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE,

ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA

US 6184389	B1	20010206	US 1995-483311	19950607	<--
AU 9661042	A1	19961230	AU 1996-61042	19960607	<--
JP 10509185	T2	19980908	JP 1996-501887	19960607	<--
EP 865439	A1	19980923	EP 1996-918360	19960607	<--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
PRAI US 1995-483311	A	19950607	<--		
US 1994-179970	A2	19940111	<--		
WO 1996-US9604	W	19960607	<--		

GI



I

AB **Combinatorial libraries** constructed to include aminodiol monomer subunits connected by phosphodiester, phosphorothioate, or phosphoramidate linking moieties were described. Thus, oligomeric compds. and **libraries** of such compds. comprising a plurality of aminodiol monomer subunits, e.g., I [R1 = TL or a protective group; L = (cyclo)alk(en)yl, aryl, heterocyclyl, etc.; R3,R4 = H, protective group, P(O)R, etc.; R = OH, (di)alkylamino, etc.; T = bond, CH2, {[CR6R7]mR5[CR8R9]n[CR10]pE}q(sic); E,R5 = bond, CH:CH, C.tplbond.C, O, NR11, etc.; R10 = O, S, NR11; R6-R9,R11 = H, (halo)alkyl, aryl, etc.; m,n = 0-5; p = 0 or 1; q = 1 to about 10 (sic)] joined by linking groups were claimed.

IT **98-88-4**, Benzoyl chloride **28920-43-6**
RL: RCT (Reactant)
(**combinatorial libraries** having aminodiol monomer subunits)

L94 ANSWER 56 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:123456 HCAPLUS
DN 126:220304
TI **Combinatorial** synthesis and biological evaluation of **library** of small-molecule Ser/Thr-**protein** phosphatase inhibitors
AU Wipf, Peter; Cunningham, April; Rice, Robert L.; Lazo, John S.
CS Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA
SO Bioorg. Med. Chem. (**1997**), 5(1), 165-177
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier
DT Journal
LA English
AB In eukaryotes, phosphorylation of serine, threonine, and tyrosine residues on **proteins** is a fundamental post-translational regulatory process for such functions as signal transduction, gene transcription, RNA splicing, cellular adhesion, apoptosis, and cell cycle control. Based on functional groups present in natural product serine/threonine **protein** phosphatase (PSTPase) inhibitors, we have designed pharmacophore model and demonstrated the feasibility of a **combinatorial chem.** approach for the prepn. of functional analogs of the model. Preliminary biol. testing of 18 structural variants of the model has identified two compds. with growth inhibitory activity against cultured human breast cancer cells. In vitro inhibition of the PSTPase PP2A was demonstrated with one of the compds.

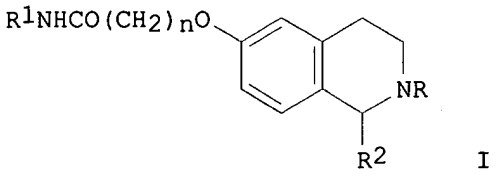
Using flow cytometry, it was obsd. that one compd. caused prominent inhibition in the G1 phase of the cell cycle. Thus, the **combinatorial** modifications of the minimal pharmacophore can generate biol. interesting antiproliferative agents.

IT **112-13-0**, Decanoyl chloride **28920-43-6**, Fmoc chloride
RL: RCT (Reactant)
(**combinatorial** synthesis and biol. evaluation of **library** of small-mol. Ser/Thr-**protein** phosphatase inhibitors)

L94 ANSWER 57 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:111529 HCAPLUS
DN 126:211642
TI Ion-exchange resins for solution phase parallel synthesis of chemical **libraries**
AU Gayo, Leah M.; Suto, Mark J.
CS Dep. Medicinal Chem., Signal Pharmaceuticals, Inc., San Diego, CA, 92121, USA
SO Tetrahedron Lett. (**1997**), 38(4), 513-516
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier
DT Journal
LA English
AB Described are various techniques that employ ion-exchange resins for the soln.-phase synthesis of chem. **libraries**. We have found these resins to be useful as reagents and/or scavengers in a variety of reactions. Nine basic ion-exchange resins were evaluated for the catalysis and purifn. of an **amide** synthesized from an **acid chloride**. A no. of the resins examd. provided products in >95% purity. Acidic ion-exchange resins were also useful as scavengers in the synthesis of ureas. A demonstration of the utility of these resins for the prepn. of **amide**, ester, and urea **libraries** is also described.

IT **5271-67-0**, 2-Thiophenecarbonyl chloride
RL: RCT (Reactant)
(use of ion-exchange resins for soln. phase parallel synthesis of chem. **libraries**)

L94 ANSWER 58 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:25886 HCAPLUS
DN 126:103989
TI 1,2,6-trisubstituted tetrahydroisoquinoline derivatives by solid-phase synthesis
AU Roelfing, K.; Thiel, M.; Kuenzer, H.
CS Research Lab., Schering A.-G., Berlin, D-13342, Germany
SO Synlett (**1996**), (11), 1036-1038
CODEN: SYNLES; ISSN: 0936-5214
PB Thieme
DT Journal
LA English
OS CASREACT 126:103989
GI



I

AB An 8-step reaction sequence for simultaneous multiple synthesis of tetrahydroisoquinolines I [n = 4, 10; R = CHMe2, pentyl; R1 = CHMe2, CH2Ph, 4-ClC6H4(CH2)2; R2 = Ph, 3-thienyl] on 2-hydroxyethyl polystyrene

was developed. Each target is comprised of a common fixed building block and 4 variable ones which are selected from 3 com. available compd. sets [.omega.-halogenated fatty acids, primary **amines**, and **acid chlorides**]. The assemblage of a prototype **library** featuring 24 discrete members serves to illustrate the protocol.

IT **98-88-4**, Benzoyl chloride
RL: RCT (Reactant)
(solid-phase synthesis of tetrahydroisoquinolines using **combinatorial library**)

L94 ANSWER 59 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:9900 HCAPLUS
DN 126:44632
TI **PILOT** [**Peptide** Identification and Lead Optimization Technique] apparatus for **peptide** synthesis and screening
IN Hudson, Derek; Johnson, Charles R.; Giebel, Lutz
PA Arris Pharmaceutical Corporation, USA
SO U.S., 78 pp. Cont.-in-part of U.S. Ser. No. 939,065.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 5585275	A	19961217	US 1993-79741	19930618	<--
	US 5591646	A	19970107	US 1992-939065	19920902	<--
	WO 9405394	A1	19940317	WO 1993-US8267	19930902	<--
	W: AU, CA, JP, NO					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	WO 9419694	A1	19940901	WO 1994-US2036	19940218	<--
	W: AU, CA, CN, JP, NO, US					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	AU 9463939	A1	19940914	AU 1994-63939	19940218	<--
	JP 08507602	T2	19960813	JP 1994-519285	19940218	<--
PRAI	US 1992-939065		19920902	<--		
	US 1993-19725		19930219	<--		
	US 1993-79741		19930618	<--		
	WO 1993-US8267		19930902	<--		
	WO 1994-US2036		19940218	<--		

AB A method and app. are disclosed for the simple and rapid prepn. of reusable, addressable surface-immobilized arrays of biomols. (**libraries**) used for screening for interaction with any biol. significant target. A special plate having on or in its surface a plurality of discreet functionalized substrate areas, typically in arrays of 10 .times. 10 to 400 .times. 400, is provided for **chem.** synthesis or bonding thereon of desired families of biomols. (e.g. **peptides**, DNA, RNA, oligosaccharides). In the case of **peptides**, such as hexapeptides, the resulting permanently hexapeptide-loaded plate is a reusable Addressable Synthetic **Peptide Combinatorial Library** (ASPCL), in which 1 to 3 (typically 2) of the positions in the sequence are uniquely identified by the address location. The preferred plate embodiment employs an HPMP wink of porous polyolefin removably received in holes in the plate. A unique multi-slot block assembly is used to prep. the ASPCLs. The wink carrier plate is also employed with a vacuum block system to assist in washing, deprotection, and probing. In **library** applications, for example detg. **peptides** which bind to functional **proteins** (enzymes, receptors, antibodies), the substrate-bound **peptides** are assembled with several positions consisting of uniformly distributed equimolar mixts. of residues, and 2 sepd. or sequential positions uniquely identified by their spatial location on the substrate array, the "address". Following identification of the known residues giving the greatest affinity for the arrayed positions in the sequence, optimal binding for the complete **peptide** sequence is detd. by an iterative process replacing

formerly mixed positions with known **amino acids** at unique addresses.

L94 ANSWER 60 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:722417 HCAPLUS
DN 126:89652
TI Parallel synthesis and screening of a solid phase carbohydrate **library**
AU Liang, Rui; Yan, Lin; Loebach, Jennifer; Ge, Min; Uozumi, Yasuhiro; Sekanina, Klara; Horan, Nina; Gildersleeve, Jeff; Thompson, Chris; et al.
CS Dep. Chem., Princeton Univ., Princeton, NJ, 08544, USA
SO Science (Washington, D. C.) (**1996**), 274(5292), 1520-1522
CODEN: SCIEAS; ISSN: 0036-8075
PB American Association for the Advancement of Science
DT Journal
LA English
AB A solid phase carbohydrate **library** was synthesized and screened against Bauhinia purpurea lectin. The **library**, which contains approx. 1200 di- and trisaccharides, was synthesized with chem. encoding on TentaGel resin so that each bead contained a single carbohydrate. Two ligands that bind more tightly to the lectin than Gal-.beta.-1,3-GalNAc (the known ligand) have been identified. The strategy outlined can be used to identify carbohydrate-based ligands for any receptor; however, because the derivatized beads mimic the polyvalent presentation of cell surface carbohydrates, the screen may prove esp. valuable for discovering new compds. that bind to **proteins** participating in cell adhesion.
IT **98-88-4**, Benzoyl chloride **108-12-3 122-04-3** **638-29-9**, Pentanoyl chloride **5271-67-0**, 2-Thiophenecarbonyl chloride
RL: RCT (Reactant)
(prepn. and screening of a solid phase oligosaccharides **library** as lectin receptors)

L94 ANSWER 61 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:672858 HCAPLUS
DN 126:18445
TI Complex **combinatorial chemical libraries** encoded with tags
IN Still, W. Clark; Wigler, Michael H.; Ohlmeyer, Michael H. J.; Dillard, Lawrence W.; Reader, John C.
PA The Trustees of Columbia University In the City of New York, USA; Cold Spring Harbor Laboratory
SO U.S., 42 pp. Cont.-in-part of U.S. Ser. No. 159,861.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5565324	A	19961015	US 1994-227007	19940413 <--
	CA 2187792	AA	19951026	CA 1995-2187792	19950413 <--
	WO 9528640	A1	19951026	WO 1995-US4683	19950413 <--
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9522926	A1	19951110	AU 1995-22926	19950413 <--
	EP 755514	A1	19970129	EP 1995-916420	19950413 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	HU 74985	A2	19970328	HU 1996-2800	19950413 <--
	CN 1151793	A	19970611	CN 1995-193518	19950413 <--
	JP 10502614	T2	19980310	JP 1995-527142	19950413 <--

	US 5721099	A	19980224	US 1995-484714	19950607 <--
	US 5968736	A	19991019	US 1995-480821	19950607 <--
	US 6001579	A	19991214	US 1995-485018	19950607 <--
	US 5789172	A	19980804	US 1996-680716	19960711 <--
	NO 9604332	A	19961203	NO 1996-4332	19961011 <--
PRAI	US 1992-955371		19921001 <--		
	US 1993-13948		19930204 <--		
	US 1993-130271		19931001 <--		
	US 1993-159861		19931130 <--		
	WO 1993-US9345		19931001 <--		
	US 1994-227007		19940413 <--		
	WO 1995-US4683		19950413 <--		

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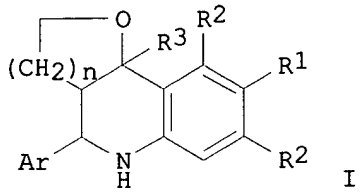
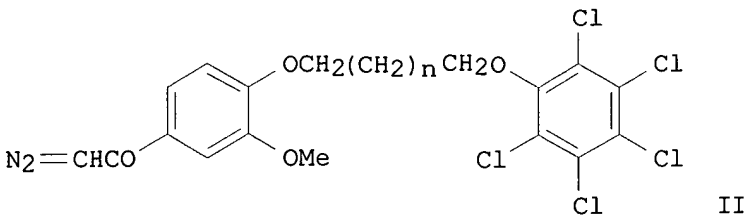


I



II

AB Encoded **combinatorial chem.** is provided, where sequential synthetic schemes are recorded using org. mols., which define choice of reactant, and stage, as the same or different bit of information. Various products can be produced in the multi-stage synthesis, such as oligomers and synthetic non-repetitive org. mols. Conveniently, nested families of compds. can be employed as identifiers, where no. and/or position of a substituent define the choice. Alternatively, detectable functionalities may be employed, such as radioisotopes, fluorescers, halogens, and the like, where presence and ratios of two different groups can be used to define stage or choice. Particularly, pluralities of identifiers may be used to provide a binary or higher code, so as to define a plurality of choices with only a few detachable tags. The particles may be screened for a characteristic of interest, particularly binding affinity, where the products may be detached from the particle or retained on the particle. The reaction history of the particles which are pos. for the characteristic can be detd. by the release of the tags and anal. to define the reaction history of the particle. For example, a **combinatorial** hetero-Diels-Alder **library** of 42 compds. I [R1 = H, MeO, CF3, OCF3, OPh, cyclohexyl; R2 = H, Me, OMe; R3 = H when n = 2, R3 = Me when n = 1; Ar = 4-HOC6H4, 2,4-Cl(HO)C6H3, 2-hydroxy-1-naphthyl] was prepd. in 6 steps. on polystyrene beads. The beads were tagged in the 3rd, 4th, and 5th steps using various combinations of the 7 identifier mols. II [n = 10-4, indicated by letters a-g, resp.] to indicate the nature of the variable groups. The tags were cleaved from the beads by oxidn. with ceric ammonium nitrate, and were analyzed by gas chromatog. with electron-capture detection. One of 4 randomly selected beads showed the presence of both tags IIa and IIb [coding for Ar = 2-hydroxy-1-naphthyl], all 3 tags IIc, IId, and IIe [coding for R1 = cyclohexyl and R2 = H], and

IIf but not IIg [coding for R3 = Me and n = 1]. Addnl. examples illustrate prepns. of various tags/identifiers, and prepn. of benzodiazepine **libraries** (prophetic) and **peptide/amide libraries**. **Peptide libraries** with 2401 and 117,647 members were encoded using only 12 and 18 identifiers, resp., and a mixed **peptide/amide library** with 23,540,625 members was encoded using only 25 identifiers.

IT **75-44-5**, Carbonic dichloride
RL: RCT (Reactant)
(tag precursor; complex **combinatorial chem.** **libraries** encoded with tags)

L94 ANSWER 62 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:660965 HCAPLUS
DN 125:301496
TI Preparation of carbopeptoids, carbonucleotides, and **libraries** thereof.
IN Nicolaou, Kyriacos C.
PA Scripps Research Institute, USA
SO PCT Int. Appl., 176 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9627379	A1	19960912	WO 1996-US3227	19960308	<--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI					
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN					
	CA 2214789	AA	19960912	CA 1996-2214789	19960308	<--
	AU 9651882	A1	19960923	AU 1996-51882	19960308	<--
	AU 717099	B2	20000316			
	EP 827406	A1	19980311	EP 1996-908737	19960308	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI					
	US 6204376	B1	20010320	US 1997-913035	19971120	<--
PRAI	US 1995-401039	A2	19950308	<--		
	WO 1996-US3227	W	19960308	<--		

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A1CONHA2 (A1 = carbohydrate **amino acid** subunit having an anomeric C bonded to the carbonyl C of the **amide** linkage; A2 = carbohydrate **amino acid** bonded to the amido N of the **amide** linkage), and G1OP(O)(OHO)G2 (G1 = carbohydrate C-glycoside having an anomeric C forming a C-glycosidic bond to the phosphodiester linkage; G2 = carbohydrate C-glycoside having a non-anomeric C bonded to the phosphodiester linkage), were prepd. Thus, title compd. (I) was prepd. by iterative coupling of phosphoramidite units (II; TBS = tert-butyldimethylsilyl; Bn = PhCH2) (prepn. given) with naphthoate ester (III) (prepn. given).

IT **89992-70-1**, 2-Cyanoethyl-N,N-diisopropylchlorophosphoramidite
RL: RCT (Reactant)
(prepn. of carbopeptoids, carbonucleotides, and **libraries** thereof)

L94 ANSWER 63 OF 83 HCAPLUS COPYRIGHT 2001 ACS

AN 1996:609917 HCAPLUS
DN 125:248492
TI Preparation of **peptides** and compounds that bind to SH2 (src homology region 2) domains of **proteins** and methods for their identification
IN Patel, Dinesh V.; Gordeev, Mikhail F.; Gordon, Eric; Grove, J. Russell; Hart, Charles P.; Kim, Moon H.; Szardenings, Anna Katrin
PA Affymax Technologies N.V., Neth.
SO PCT Int. Appl., 204 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9623813	A1	19960808	WO 1996-US1544	19960131 <--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE				
	AU 9649720	A1	19960821	AU 1996-49720	19960131 <--
PRAI	US 1995-382100		19950201 <--		
	WO 1996-US1544		19960131 <--		

AB SH2-binding **peptides** comprising a core sequence of **amino acids** Z7XZ8X (X = a member independently selected from the group consisting of the 20 genetically coded L-**amino acids** and the stereoisomeric D-**amino acids**; Z7 = phosphotyrosine or an isostere thereof; Z8 = asparagine or an isostere thereof; the **amino acid** terminus is acylated; the **peptide** is less than 14 **amino acids**; provided that if Z7 is phosphotyrosine and Z8 is asparagine, then the **peptide** is not GDGZ7XZ8XPLL), which bind to the SH2 domain or domains of various **proteins**, are prepd. These **peptides** and compds. have application as agonists and antagonists of SH2 domain contg. **proteins**, and as diagnostic or. A **library** of **peptides** bound to a solid support, useful for identifying ligands capable of binding to SH2 domains, is also prepd. therapeutic agents for the diagnosis or treatment of disease conditions. A method for identifying an SH2-binding **peptide** comprises contacting the resp. members of a **library** with an SH2 domain contg. **protein** or SH2 domain fragment and identifying SH2-binding **peptides** on the basis of a binding affinity of .ltoreq.1 .times. 10-4 M. In particular, a method for treating a disease assocd. with aberrant cell growth, differentiation, or regulation which is assocd. with defects in receptor tyrosine kinase pathways comprises administering to a patient above **peptide** in an amt. sufficient to partially block or inhibit a cellular signal transduction pathway. Said disease is selected from cancer, developmental and differentiation disease, and insulin-resistant (or non-insulin dependent) diabetes. Thus, a phosphotyrosine-contg. **peptide library** on a solid support with the general sequence A-pY-X1-X2-X3-S-V (pY = phosphotyrosine residue, X1 - X3 = Ala, Arg, Asn, Asp, Glu, Gln, Gly, His, Ile, Leu, Lys, Met, Phe, Pro, Ser, Thr, Val, Tyr, Trp, Vvl, Nle, etc.) representing 17,576 **peptides** was prepd. and one of the **library** sequence (ApYLNESV) showed greater affinity for the SH2 domain than did the pos. control sequence (ApYINQSV, residue from the SH2-binding domain of human EGF) (4.5 .mu.M vs. 12 .mu.M).

IT **79-37-8**, Oxalyl chloride **28920-43-6**, 9-Fluorenylmethoxycarbonyl chloride
RL: RCT (Reactant)
(prepn. of **peptides** and **peptide library** having binding affinity to SH2 domains for diagnosis and treatment of diseases)

L94 ANSWER 64 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:578083 HCAPLUS
DN 125:240778
TI Discovery of a herbicidal lead using polymer-bound activated esters in generating a **combinatorial library** of **amides** and esters
AU Parlow, John J.; Normansell, Jean E.
CS Ceregen Div. Monsanto Co., St. Louis, MO, 63167, USA
SO Mol. Diversity (**1996**), 1(4), 266-269
CODEN: MODIF4; ISSN: 1381-1991
DT Journal
LA English
AB A **combinatorial library** contg. mixts. of **amides** and esters was prepd. through solid-phase **chem.** The advantages of using solid-phase **chem.** over soln.-phase **chem.** to prep. this **library** are discussed. The **library** was screened through a **high-throughput** whole organism herbicidal assay upon which a mixt. contg. **amides** was found to have herbicidal activity. Deconvolution of the mixt. provided N-(3-benzoylphenyl)-3-(1,1-dimethylethyl)-1-methyl-1H-pyrazole-5-carboxamide as a herbicidal lead with broadleaf and narrowleaf pre-emergence herbicidal activity as low as 100 g/ha on some weed species. This study represents the first report of an agrochem. discovered using a **combinatorial** approach.

L94 ANSWER 65 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:548554 HCAPLUS
DN 125:194633
TI Methods for production of large cataloged chemical **libraries**
IN Peterson, John R.; Garr, Cheryl D.; Miller, Jon P.
PA Panlabs, Inc., USA
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9621859	A1	19960718	WO 1996-US94	19960111 <--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD				
	CA 2210071	AA	19960718	CA 1996-2210071	19960111 <--
	AU 9646522	A1	19960731	AU 1996-46522	19960111 <--
	AU 697473	B2	19981008		
	EP 803063	A1	19971029	EP 1996-902071	19960111 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
	CN 1173921	A	19980218	CN 1996-191914	19960111 <--
	JP 11500419	T2	19990112	JP 1996-521733	19960111 <--
PRAI	US 1995-371543		19950111 <--		
	WO 1996-US94		19960111 <--		

AB The invention provides cataloged chem. **libraries** contg. a multiplicity of reaction products and that are useful for screening for a variety of uses including for pharmacol. activity, providing pharmacol. leads, optimization of lead selection, screening for herbicides, pesticides and the like. The chem. **libraries** are produced by semi-automated and automated soln. chem. methods and have a cataloging system using an electronic database which allows ready storage and access to a variety of useful information about any of the reaction products.

L94 ANSWER 66 OF 83 HCAPLUS COPYRIGHT 2001 ACS

AN 1996:548550 HCAPLUS
DN 125:195992
TI Non-nucleotide phosphorus ester oligomers
IN Gentles, Robert G.; Cook, Alan F.; Rudolph, M. Jonathan; Fathi, Reza
PA Pharmagenics, Inc., USA
SO PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9622297	A1	19960725	WO 1996-US369	19960103 <--
	W: AU, CA, JP				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5919965	A	19990706	US 1995-374040	19950118 <--
	CA 2210759	AA	19960725	CA 1996-2210759	19960103 <--
	AU 9648969	A1	19960807	AU 1996-48969	19960103 <--
	AU 701299	B2	19990121		
	EP 804443	A1	19971105	EP 1996-905134	19960103 <--
	R: CH, DE, FR, GB, IT, LI, SE				
	JP 10512569	T2	19981202	JP 1996-522322	19960103 <--
PRAI	US 1995-374040		19950118 <--		
	WO 1996-US369		19960103 <--		

OS MARPAT 125:195992
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A P ester oligomer having structure I wherein A can be the same or different in each monomeric unit and each is independently selected from the group consisting of O, S, lower alkyl, alkyl- or aryl-substituted amino and aminoalkyl; B1 and B2 can be the same or different and each is independently selected from H, lower alkyl, a labeling group, a protecting group, a phosphoramidate or a phosphomonoester; R1 can be the same or different in each monomeric unit, and in at least one of the nonnucleotide monomeric units, R1 is independently selected from the group consisting of a condensation product of (i) a nonvicinal diol attached to the H bond donor functionality; (ii) a H bond acceptor selected from an ether, a purine or pyrimidine substituted 1,2-diol or disubstituted heterocycle; (iii) a nonvicinal diol attached to a hydrophobic functionality or a vicinal diol attached to an aliph. or alicyclic hydrophobic functionality; (iv) a diol attached to a ring substituted anionic functionality and (v) a cationic moiety attached to a nonvicinal or alicyclic diol, any of which can further include a detectable label, and n is at least one. Preferred R1 moieties include condensation products of heterocyclic diols, alicyclic diols, and polycyclic diols. Also the nonnucleotide monomers thereof, **combinatorial library** mixts. of the oligomers and the use of the oligomers as selective target-binding compds. are described. An example of a simple oligomeric phosphodiester which was synthesized is II.

IT **89992-70-1**
RL: RCT (Reactant)
(prepn. of nonnucleotide monomers and **combinatorial library** mixts. of phosphorus ester oligomers)

L94 ANSWER 67 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:544189 HCAPLUS
DN 125:236878
TI **Combinatorial** Approach to the Discovery of Novel Coordination Complexes
AU Francis, Matthew B.; Finney, Nathaniel S.; Jacobsen, Eric N.
CS Department of Chemistry, Harvard University, Cambridge, MA, 02138, USA

SO J. Am. Chem. Soc. (**1996**), 118(37), 8983-8984
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA English
AB Metal complexes are reported as formed using a **library** from **combinatorial chem.** The **library** was prepd. on poly(ethylene glycol)-grafted polystyrene so that each polymer bead displayed a unique ligand structure. The **library** theor. consisted of 12,000 different ligands. It comprises 4 variable components: 2 **amino acids** linked by a "turn element" and terminated by various capping reagents. The turn elements employed were cyclic 1,2-amino alcs. or .alpha.-**amino acid** derivs. Metals used were Ni, Fe, Cu, Pt, Sn, and Pd. With Ni, 4 different ligands were found each bearing L-His(Trt) in both **amino acid** positions; only 2 turn elements, acetyl and 1-naphthylenyl chlorides, were found. Extent of binding is reported for the other metals with some general observations regarding selectivity of **amino acids.**
IT **75-36-5D**, Acetyl chloride, **amino acid** deriv.
transition metal complexes poly(ethylene glycol)-grafted polystyrene-supported
RL: FMU (Formation, unclassified); FORM (Formation, nonpreparative)
(metal binding by **amino acid** deriv.
polymer-supported ligands from combinatorial synthesis)

L94 ANSWER 68 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:369153 HCAPLUS
DN 125:34037
TI Preparation of soluble **combinatorial libraries** using soluble macromolecular supports
IN Janda, Kim; Han, Hyunsoo
PA Scripps Research Institute, USA
SO PCT Int. Appl., 154 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9603418	A1	19960208	WO 1995-US9614	19950726 <--
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2195321	AA	19960208	CA 1995-2195321	19950726 <--
	AU 9532722	A1	19960222	AU 1995-32722	19950726 <--
	AU 697920	B2	19981022		
	EP 772623	A1	19970514	EP 1995-929334	19950726 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 10506379	T2	19980623	JP 1995-505990	19950726 <--
PRAI	US 1994-281200		19940726 <--		
	US 1995-484153		19950607 <--		
	WO 1995-US9614		19950726 <--		

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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Novel sol. **combinatorial libraries** are prepd., comprising a sol. phase in soln. attached to a core mol., and allowing the improved high-yield and efficient prodn. of sol. **combinatorial**

libraries. Some specific examples of the sol. **combinatorial libraries** claimed herein comprise one or more of the following: **amino acids**, .alpha.-azetide **amino acids**, triazine dione mols., .gamma.-lactamtide mols. (constrained **peptide** mimics), .delta.-lactamthiotide mols. (constrained **peptide** mimics), .beta.-lactam nucleus contg. mols., lycoramine alkaloid nucleus contg. mols., .beta.-blocker nucleus mols., oligopeptides, oligosaccharides, oligonucleotides, and arylsulfonamides. The macromol. supports are selected from polyethylene glycol, polyvinyl alc., polyvinylamine copolymd. with polyvinylpyrrolidine, and derivs. thereof. Further, a split synthesis technique for generating **libraries** of **combinatorial** mols. employs a biphasic macromol. support which is sol. during the pooling, splitting, and coupling steps but which is insol. during the washing step. The use of a biphasic macromol. support in its insol. phase significantly enhances the efficiency and performance of the washing step. Thus, a **library** of 8 tetrasaccharides (e.g. I, II, and III), useful as antigenic markers which distinguishes fetal erythrocytes from adult cells (no data), were prepd. by the split synthesis technique involving sequential coupling of a **library** of polyethylene glycol monomethyl ether-bound glucose and galactose derivs. (IV and V; R = MeO-PEG-O2CCH2CH2CO, wherein PEG = polyethylene glycol) (prepn. given) with (A) galactosamine and glucosamine derivs. (VI and VII) (prepn. given), (B) glucose and galactose derivs. IV and V (R = H) (prepn. given), and (C) galactosamine deriv. VI.

IT **75-44-5**, Phosgene
RL: RCT (Reactant)
(prepn. of sol. **combinatorial libraries** using sol. macromol. supports)

L94 ANSWER 69 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:175910 HCAPLUS
DN 124:342182
TI Versatile Approach To Encoding **Combinatorial** Organic Syntheses Using **Chemically** Robust Secondary **Amine** Tags
AU Ni, Zhi-Jie; Maclean, Derek; Holmes, Christopher P.; Murphy, Martin M.; Ruhland, Beatrice; Jacobs, Jeffrey W.; Gordon, Eric M.; Gallop, Mark A.
CS Affymax Research Institute, Palo Alto, CA, 94304, USA
SO J. Med. Chem. (**1996**), 39(8), 1601-8
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
AB Encoded **combinatorial** org. synthesis has recently emerged as a powerful tool for the discovery of biol. active compds. from complex **chem. libraries**. This report describes a new encoding methodol. that uses **chem**. robust secondary **amines** as tags. These **amines** are incorporated into an N-[(dialkylcarbamoyl)methyl]glycine-coding oligomer through simple **chem**. that is compatible with a wide range of polymer-supported transformations useful in **combinatorial** synthesis. In the decoding process acidic hydrolysis of the tagging polymer regenerates the secondary **amines**, which after dansylation are resolved and detected at sub-picomole levels by reversed-phase HPLC. The versatility of this strategy is demonstrated here by encoded syntheses of members of several representative heterocyclic compd. classes, including .beta.-lactams, 4-thiazolidinones, and pyrrolidines.

IT **701-99-5**, Phenoxyacetyl chloride
RL: RCT (Reactant)
(prepn. of **combinatorial libraries** of org. compds. using **chem**. robust secondary **amine** tags)

L94 ANSWER 70 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:114374 HCAPLUS
DN 124:261653
TI Solid phase synthesis of hydantoins using a carbamate linker and a novel cyclization/cleavage step

AU Dressman, Bruce A.; Spangle, Larry A.; Kaldor, Stephen W.
CS Lilliy Res. Lab., Lilly Corporate Center, Indianapolis, IN, 46285, USA
SO Tetrahedron Lett. (**1996**), 37(7), 937-40
CODEN: TELEAY; ISSN: 0040-4039
DT Journal
LA English
AB An 800 compd. hydantoin **library** has been constructed using a diverse set of 20 **amino acids** and over 80 primary **amines**. **Amino acids** were attached via their N-termini to (hydroxymethyl)polystyrene using a carbamate linker. Bound **amino acids** were converted to their corresponding **amides** and then cyclized under basic conditions to give hydantoins in high purities.
IT **7693-46-1**, p-Nitrophenyl chloroformate
RL: RCT (Reactant)
(solid phase synthesis of hydantoins using a carbamate linker and a novel cyclization/cleavage step)
IT **7693-46-1DP**, p-Nitrophenyl chloroformate, reaction products with (hydroxymethyl)polystyrene
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(solid phase synthesis of hydantoins using a carbamate linker and a novel cyclization/cleavage step)

L94 ANSWER 71 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:34696 HCAPLUS
DN 124:116916
TI Solid-Supported **Combinatorial** Synthesis of Structurally Diverse .beta.-Lactams
AU Ruhland, Beatrice; Bhandari, Ashok; Gordon, Eric M.; Gallop, Mark A.
CS Affymax Research Institute, Palo Alto, CA, 94304, USA
SO J. Am. Chem. Soc. (**1996**), 118(1), 253-4
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA English
AB This communication describes the prepn. of .beta.-lactams via a [2+2] cycloaddn. reaction of ketenes to resin-bound imines derived from **amino acids**. This solid-phase adaptation of the Staudinger reaction has been used to prep. **combinatorial libraries** of 3,4-bis-substituted 2-azetidinones, and provides a novel approach to the synthesis of N-unsubstituted-.beta.-lactams, important building blocks for the prepn. of .beta.-lactam antibiotics and useful precursors of chiral .beta.-**amino acids**.
IT **701-99-5**, Phenoxyacetyl chloride
RL: RCT (Reactant)
(**combinatorial library** of .beta.-lactams via Staudinger reaction of resin-bound imines)

L94 ANSWER 72 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:1005479 HCAPLUS
DN 124:176900
TI **Protein** Structure-Based Design of **Combinatorial Libraries**: Discovery of Non-**Peptide** Binding Elements to Src SH3 Domain
AU Combs, Andrew P.; Kapoor, Tarun M.; Feng, Sibo; Chen, James K.; Daude-Snow, Lygia F.; Schreiber, Stuart L.
CS Howard Hughes Medical Institute, Harvard University, Cambridge, MA, 02138, USA
SO J. Am. Chem. Soc. (**1996**), 118(1), 287-8
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA English
AB An approach to the discovery of cell permeable ligands to **protein** receptors is reported. By examg. the 3-dimensional structures of SH3-**peptide** complexes detd. by multidimensional NMR, a solid phase, encoded combinatorial synthesis was rationally designed to deliver nonpeptide binding elements to the site of a key specificity-detg. pocket

in SH3 domains. Fifteen ligands to the SH3 domain from the **protein** tyrosine kinase Src were selected from a pool of >1,000,000 spatially sepd. mols. These were resynthesized and individually analyzed for their ability to bind to the Src SH3 domain. They were shown to be among the highest affinity SH3 ligands known, and they are the first SH3 ligands to use nonpeptide binding elements. The strategy used in this study is expected to be applicable to the discovery of ligands to **proteins** in general in general.

IT **108-12-3**, Isopentanoyl chloride **108-23-6**, Isopropyl chloroformate **543-27-1**, Isobutyl chloroformate **701-99-5**, Phenoxyacetyl chloride **874-60-2**, 4-Methylbenzoyl chloride **2719-27-9**, Cyclohexanecarbonyl chloride **4521-61-3**, 3,4,5-Trimethoxybenzoyl chloride **5271-67-0**, 2-Thiophenecarbonyl chloride
RL: RCT (Reactant)
(**protein** structure-based design of **combinatorial libraries** discovery of nonpeptide binding elements to Src SH3 domain)

L94 ANSWER 73 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:994352 HCAPLUS
DN 124:146747
TI Preparation of novel phosphoramidate and phophorothioamidate oligomeric compounds
IN Cook, Phillip Dan; Acevedo, Oscar; Hebert, Normand
PA Isis Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9523160	A1	19950831	WO 1995-US2267	19950223	<--
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN					
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
	US 5637684	A	19970610	US 1994-200638	19940223	<--
	CA 2184005	AA	19950831	CA 1995-2184005	19950223	<--
	AU 9519691	A1	19950911	AU 1995-19691	19950223	<--
	AU 677150	B2	19970410			
	EP 751948	A1	19970108	EP 1995-912595	19950223	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
	JP 09509663	T2	19970930	JP 1995-522463	19950223	<--
	JP 2972344	B2	19991108			
	US 5717083	A	19980210	US 1996-693112	19960819	<--
PRAI	US 1994-200638		19940223	<--		
	WO 1995-US2267		19950223	<--		

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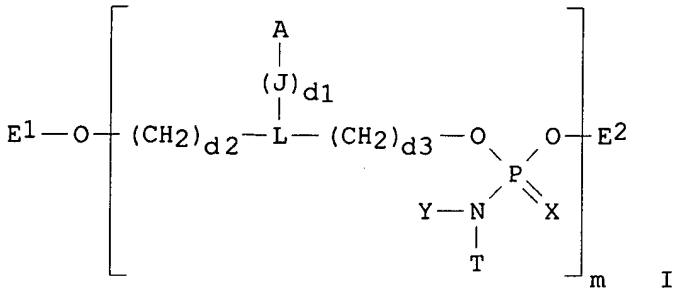

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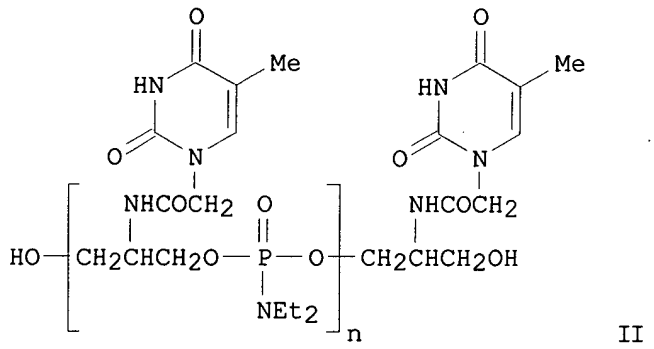


II

AB The title compds.[I; L = backbone segments; Y, T, A = functional groups for (non)interacting with target mols. of interest such as a N-contg. heterocycle, purine, pyrimidine, phosphate, polyether, and polyethylene glycol; X = O, S; E1, E2 = H, conjugate groups or intermediate groups used during the synthesis of the compds.; J = linking group such as C1-20 alkyl, CO, C(S), CO2, and CONH; d1 = 0,1; d2 = 0-6; d3 = 1-6; m = 2-50], useful as inhibitors of phospholipase A2, are prepd. using H phosphonate type chem. wherein the functional groups are added during an oxidn. step or during a coupling step. Thus, a thymine-contg. oligomer (II) was prepd. by repeating the steps involving coupling of 1-O-(4,4'-dimethoxytrityl)-N-(9-fluorenylmethoxycarbonyl)-3-amino-1,3-propanediol 3-O-phosphonate to 1-O-(4,4'-dimethoxytrityl)-N-(1-thymin-1-ylacetyl)-2-amino-1,3-propanediol 3-succinate-bound long chain-alkylamino control pore glass support, oxidn. of the resulting H phosphonate with Et2NH to the phosphoramidate, removing the Fmoc-protective group, and reacting the free **amine** with 1-carboxymethylthymine. Oligomer **libraries** were also prepd. (only general prepn. given) and screened for inhibition of phospholipase A2 using Escherichia coli labeled with 3H-oleic acid to show specific inhibition for human type II phospholipase A2 (no details for biol. data given).

IT **98-88-4**, Benzoyl chloride **28920-43-6**, 9-Fluorenylmethyl chloroformate
RL: RCT (Reactant)
(prepn. of novel phosphoramidate and phophorothioamidate oligomeric compds. and **combinatorial libraries** as phospholipase A2 inhibitors)

L94 ANSWER 74 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:994345 HCAPLUS
DN 124:146851
TI Preparation of oligomeric **peptide** nucleic acid (PNA) **combinatorial libraries** and improved methods of synthesis
IN Cook, Philip Dan; Kiely, John; Sprankle, Kelly
PA Isis Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 103 pp.
CODEN: PIXXD2
DT **Patent**

LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9523163	A1	19950831	WO 1995-US2182	19950222 <--
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
	RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5539083	A	19960723	US 1994-200742	19940223 <--
	CA 2183371	AA	19950831	CA 1995-2183371	19950222 <--
	AU 9519261	A1	19950911	AU 1995-19261	19950222 <--
	AU 684152	B2	19971204		
	JP 09503523	T2	19970408	JP 1995-522421	19950222 <--
	EP 777678	A1	19970611	EP 1995-911848	19950222 <--
	EP 777678	B1	19991013		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 11209393	A2	19990803	JP 1998-322576	19950222 <--
	AT 185572	E	19991015	AT 1995-911848	19950222 <--
	US 5864010	A	19990126	US 1996-587648	19960117 <--
	US 5831014	A	19981103	US 1996-693144	19960813 <--
PRAI	US 1994-200742	A2	19940223 <--		
	JP 1995-522421	A3	19950222 <--		
	WO 1995-US2182	W	19950222 <--		

AB New sub-monomer synthetic methods for the prepn. of **peptide** nucleic acid oligomeric structures, useful as inhibitors of enzymes such as phospholipase A2 and for the treatment of inflammatory diseases including atopic dermatitis and inflammatory bowel disease (no data), are disclosed, that provide for the synthesis of both predefined sequence **peptide** nucleic acid oligomers as well as random sequence **peptide** nucleic acid oligomers. Further these methods also provide for the incorporation of **peptide** nucleic acid units or strings of such units with **amino acids** or strings of **amino acids** in chimeric **peptide** nucleic acid-**amino acid** compds. Further disclosed are methods of making random **libraries** of **peptide** nucleic acids using the fully preformed monomers. Thus, a **combinatorial library** of chimeric **peptide** nucleic acid oligomers was prepd. using 1-[(N2-benzyloxycarbonyl-N6-benzyloxy-2-aminopurin-9-yl)acetyl]-2-oxomorpholine (I), 1-[(N6-benzyloxycarbonyladenin-9-yl)acetyl]-2-oxomorpholine (II), 1-[(N4-benzyloxycarbonylcytosin-1-yl)acetyl]-2-oxomorpholine (III), and 1-(thymin-1-ylacetyl)-2-oxomorpholine (IV), which involved coupling of IV to a MBHA resin, Mitsunobu reaction of the resulting N-(thymin-1-ylacetyl)-N-(2-hydroxyethyl)glycine-MBHA resin with (Boc)2NH using Ph3P and di-Et azodicarboxylate, random coupling of the resulting N-(thymin-1-ylacetyl)-N-(2-aminoethyl)glycine-MBHA resin with a mixt. of I, II, III, and IV followed by Mitsunobu reaction for converting the terminal hydroxy group to the terminal **amine** moieties, repeating the latter procedure for extension of backbone and addn. of further nucleoside bases to complete the oligomer of the desired length, addn. of a **peptide** to the **peptide** nucleic acid unit using std. solid phase Merrifield **peptide** synthesis, and cleavage of **peptide** nucleic acid oligomers from the resin.

IT **75-44-5**, Carbonic dichloride **98-88-4**, Benzoyl chloride **598-21-0**, Bromoacetyl bromide
RL: RCT (Reactant)
(prepn. of oligomeric **peptide** nucleic acid (PNA) **combinatorial libraries** and improved methods of synthesis)

IT **75-36-5DP**, Acetyl chloride, resin-bound **598-21-0DP**, Bromoacetyl bromide, reaction product with MBHA resin
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(prepn. of oligomeric **peptide** nucleic acid (PNA) **combinatorial libraries** and improved methods of synthesis)

L94 ANSWER 75 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:969421 HCAPLUS
DN 124:7968
TI Modular design and synthesis of aminimide-containing molecules
IN Hogan, Joseph C., Jr.; Casebier, David; Furth, Paul; Tu, Cheng
PA Arqule Partners, L.P., USA
SO PCT Int. Appl., 208 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9518186	A1	19950706	WO 1993-US12612	19931228 <--
	W: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, UZ				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2179983	AA	19950706	CA 1993-2179983	19931228 <--
	AU 9460159	A1	19950717	AU 1994-60159	19931228 <--
	AU 689764	B2	19980409		
	EP 737232	A1	19961016	EP 1994-906465	19931228 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 09510693	T2	19971028	JP 1993-517995	19931228 <--
	CN 1105355	A	19950719	CN 1993-121725	19931230 <--
PRAI	WO 1993-US12612		19931228 <--		

OS CASREACT 124:7968
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The design and synthesis of a variety of aminimide-derived mol. modules and their use in the construction of new mols. and fabricated materials is disclosed. The new mols. and fabricated materials are mol. recognition agents useful in the design and synthesis of drugs, and have applications in sepns. and materials science. Examples given include monomers/polymers, drug conjugates, mimetics of **peptides**, (oligo)nucleotides, carbohydrates, and lipids, and a **combinatorial library** (matrix of 16). For instance, the (uridylmethyl)propylhydrazine I was acylated with acetyl chloride and alkylated with tert-Bu bromoacetate to give the aminimide II, which was deprotected with CF3CO2H. The resulting acid was used to perform a similar acylation of a similarly prepd. (cytidylmethyl)propylhydrazine, followed by another alkylation with tert-Bu bromoacetate. A 3rd cycle using I gave the tris(aminimide) III, which presents the sequence U-C-U as a recognition sequence for the RNA codon A-G-A.

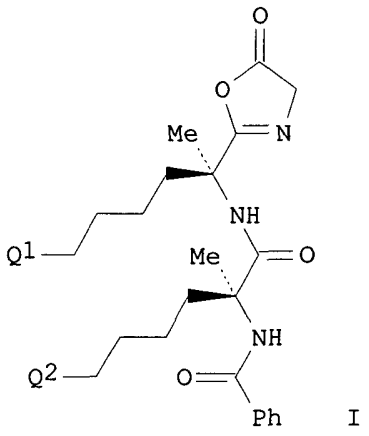
IT **75-36-5**, Acetyl chloride **79-04-9**, Chloroacetyl chloride **99-33-2**, 3,5-Dinitrobenzoyl chloride **598-21-0**, Bromoacetyl bromide
RL: RCT (Reactant)
(reactant; prepn. of aminimide-contg. mols.)

L94 ANSWER 76 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:960192 HCAPLUS
DN 124:9464
TI Modular design and synthesis of oxazolone-derived molecules.
IN Hogan, Joseph C., Jr.; Casebier, David; Furth, Paul; Tu, Cheng
PA Arqule Partners, L.P., USA
SO PCT Int. Appl., 173 pp.

CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9517903	A1	19950706	WO 1993-US12591	19931228 <--
W: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US, UZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2179984	AA	19950706	CA 1993-2179984	19931228 <--
AU 9460499	A1	19950717	AU 1994-60499	19931228 <--
EP 738155	A1	19961023	EP 1994-907107	19931228 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1105353	A	19950719	CN 1993-121726	19931230 <--
PRAI WO 1993-US12591		19931228 <--		

GI



I

AB AX[NHCRR1COG]nYB [A, B = bond, H, electrophilic or nucleophilic group, **amino acid**, nucleotide, or carbohydrate deriv., org. structural motif, reporter element, polymerizable org. group, macromol. component, R; A and B are optionally connected to each other or to other structures; X, Y = bond, .gtoreq.1 C, N, S, O atom or combinations thereof; R, R1 = A, B, cyano, NO2, halo, O, OH, alkoxy, thio, alkyl, (substituted) (hetero)aryl, etc.; G = connecting group, bond; n .gtoreq.1; with provisos], were prepd. The new mols. and fabricated materials are mol. recognition agents useful in the design and synthesis of drugs, and have applications in sepns. and materials science. Thus, oligomer (I; Q1 = 4-benzoylcytidinyl; Q2 = 4-benzoyladeninyl) was prepd. in several steps using 2-phenyl-5-oxazolone.

IT **99-33-2**, 3,5-Dinitrobenzoyl chloride **814-68-6**, Acryloyl chloride
RL: RCT (Reactant)
(modular design and synthesis of oxazolone-derived mols.)

L94 ANSWER 77 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:909471 HCAPLUS
DN 123:287310
TI Methods for synthesizing oligomers from hydroxy acids
IN Williams, Simon F.; Peoples, Oliver P.
PA Metabolix, Inc., USA
SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DT **Patent**

LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9518781	A1	19950713	WO 1995-US191	19950106 <--
	W: AU, CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9515600	A1	19950801	AU 1995-15600	19950106 <--
	US 5625030	A	19970429	US 1995-561139	19951120 <--
PRAI	US 1994-178141		19940106 <--		
	WO 1995-US191		19950106 <--		

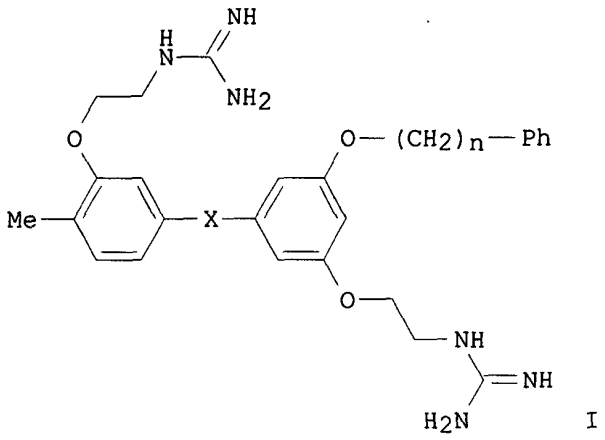
AB A process is developed to synthesize oligomeric compds. from hydroxy acids and optionally other types of monomers, such as **amino acids**, carbohydrates, nucleotides, and **peptides**. The method is rapid, simple, and readily to be automated, and useful in building a **combinatorial library** for pharmaceutical, **chem.**, and biol. screening. The process includes steps: (1) selecting a first hydroxy acid, (2) protecting either the carboxy end or the hydroxy end of the first monomer, (3) selecting a second hydroxy acid, (4) protecting the terminal group which is different to that is protected in the first monomer, (5) protecting any functional side groups, (6)linking the first monomer to a solid support via the protecting group, (7) linking the first monomer and the second monomer through the unprotected terminal group to form an oligomer bound to a solid support.

IT **28920-43-6**, 9-Fluorenylmethyl chloroformate
RL: RCT (Reactant)
(methods for synthesizing oligomers from hydroxy acids)

L94 ANSWER 78 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:789146 HCAPLUS
DN **123:198439**
TI Method for preparing and selecting pharmaceutically useful non-**peptide** compounds from a structurally diverse universal **library**
IN Pavia, Michael Raymond; Whitesides, George McClelland; Hangauer, David Garry, Jr.; Hediger, Mark Edward
PA Sphinx Pharmaceuticals Corp., USA
SO PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9504277	A1	19950209	WO 1994-US7780	19940707 <--
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ, VN				
	RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2168886	AA	19950209	CA 1994-2168886	19940707 <--
	AU 9473293	A1	19950228	AU 1994-73293	19940707 <--
	EP 712493	A1	19960522	EP 1994-923427	19940707 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 09504511	T2	19970506	JP 1994-505836	19940707 <--
	ZA 9405731	A	19950307	ZA 1994-5731	19940802 <--
PRAI	US 1993-101074		19930803 <--		
	US 1994-239542		19940508 <--		
	WO 1994-US7780		19940707 <--		

OS MARPAT 123:198439
GI



I

AB Methods are described for rapidly generating large, rationally designed **libraries** of structurally diverse, low-mol.-wt. compds., using a multicombinatorial approach. More specifically, the method concerns prepn. of **libraries** of certain biphenyl derivs., or analogous concatenated bicyclic arom. or heteroarom. systems, in several steps, including: (1) providing a solid support with a cleavable linker; (2) prepg. a 1st "scaffold", which is a substituted benzene or analogous unit bearing moieties suitable for coupling to both the support and a 2nd scaffold; (3) coupling the 1st scaffold to the support via the linker; (4) prepg. a 2nd scaffold which bears a moiety for linking to the 1st scaffold; (5) coupling the 2nd scaffold to the 1st; and (6) cleaving the final product from the linker on the support. The method, including addnl. steps for modification of functional groups in both the unattached and attached scaffolds, was applied to prepn. of compds. I [X = bond, n = 1; X = C.tplbond.C, CH:CH, CH2CH2, CH2, n = 2], which are potential bradykinin antagonists (no data).

IT **98-88-4**, Benzoyl chloride
RL: RCT (Reactant)
(starting material; prepn. of biphenyl derivs. and analogs via **combinatorial library** method)

L94 ANSWER 79 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:784846 HCAPLUS
DN 123:190480
TI Methods for isolation of most abundant oligonucleotides from complex mixtures
IN Beutel, Bruce A.; Coppola, George R.; Sherman, Michael I.; Cook, Alan F.; Fathi, Reza; Gao, Hetian; Rudolph, M. Jonathan; Bertelsen, Arthur H.
PA Pharmagenics, Inc., USA
SO PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9506751	A1	19950309	WO 1994-US9728	19940826 <--
	W: AU, CA, JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9477170	A1	19950322	AU 1994-77170	19940826 <--
PRAI	US 1993-115470		19930901 <--		
	WO 1994-US9728		19940826 <--		

AB The method of the present invention allows for screening of very large **libraries** of nucleic acids but does not require the reiterative PCR and binding steps customary in prior art methods. Instead there is only a single exposure to target followed by steps designed to identify

those sequence that are most abundant in the selected mixt. Thus, double-stranded nucleic acids present in a mixt. thereof are converted to individual strands which are renatured under conditions which favor reannealing of the nucleic acids present at higher than av. concns. in the original mixt. The procedure can be used for identifying nucleic acids which bind to a target mol. or other compds. which bind to a target mol. (such as **peptides** or modified oligonucleotides) by using nucleic acids as a coding portion of a chimeric mol. which includes such compds. These chimeric mols. could be a **combinatorial library** comprising mols. contg. sep. target-binding and coding portions as described by Brenner and Lerner (Proc. Natl. Acad. Sci., 1992). A solid phase contg. a branched linker mol., one reactive group being protected with dimethoxytrityl and one with FMOC, was prepd. This modified matrix allows selective synthesis of, for example, an oligonucleotide on either arm of the linker. Such a matrix was used to prep. an RNA **combinatorial library** and the enrichment method of the invention was used to identify RNA mols. with high affinity for basic fibroblast growth factor.

IT **28920-43-6**, 9-Fluorenylmethoxycarbonyl chloride **89992-70-1**, 2-Cyanoethyl N,N-diisopropylchlorophosphoramidite
RL: RCT (Reactant)
(prepn. of solid matrix with branched linker for construction of **combinatorial libraries**)

L94 ANSWER 80 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:517469 HCAPLUS
DN 123:55085
TI A strategy for urea linked diamine **libraries**
AU Hutchins, Steven M.; Chapman, Kevin T.
CS Dep. of Molecular Design and Diversity, Merck Res. Laboratories, Rahway, NJ, 07065, USA
SO Tetrahedron Lett. (**1995**), 36(15), 2583-6
CODEN: TELEAY; ISSN: 0040-4039
DT Journal
LA English
AB A strategy for urea linked diamine **libraries** has been developed. The route involves the use of unprotected diamines and a p-nitrophenyl carbamate intermediate for the generation of the urea. The products obtained after 8 steps are of high chem. purity.

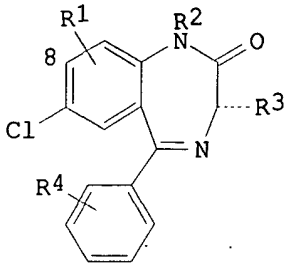
IT **7693-46-1DP**, p-Nitrophenyl chloroformate, reaction products with resin-bound **amines**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(solid-phase synthetic method for urea linked diamine **libraries** using unprotected diamines and resin-bound p-nitrophenyl carbamate intermediates)

L94 ANSWER 81 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1994:409430 HCAPLUS
DN 121:9430
TI Solid phase and **combinatorial** synthesis of benzodiazepine compounds on a solid support
IN Ellman, Jonathan A.
PA Regents of the University of California, USA
SO U.S., 25 pp.
CODEN: USXXAM
DT **Patent**
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	US 5288514	A	19940222	US 1992-944469	19920914	<--
	WO 9406291	A1	19940331	WO 1993-US8709	19930913	<--

W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,

BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
US 5545568 A 19960813 US 1993-161677 19931202 <--
PRAI US 1992-944469 19920914 <--
GI



I

AB The invention provides a rapid approach for **combinatorial** synthesis and screening of **libraries** of derivs. of therapeutically important classes of compds. such as benzodiazepines, prostaglandins, and .beta.-turn mimetics. A general methodol. for the solid-phase synthesis of these derivs. is provided. For example, in the case of 1,4-benzodiazepines such as I [R1 = H, 8-CO2H; R2 = H, Me, Et, allyl, CH2Ph; R3 = Me, CH2C6H4OH-4, iso-Pr, CH2CO2H, CH2Ph, (CH2)4NH2; R4 = H, 4-OH], a substituted, N-FMOC-protected 2-aminobenzophenone is coupled via another functional group to a solid support, preferably by a cleavable linker. After deprotection of N, the bound aminobenzophenone reacts with an FMOC-protected **amino acid** (natural or unnatural), followed by base-catalyzed deprotection of the FMOC group and acid-catalyzed cyclization, to give a benzodiazepinone deriv. This may undergo further N-alkylation. By varying the aminobenzophenones, **amino acids**, and alkylating agents, using, e.g., pin-based, bead-based, or light-directed synthetic techniques, a plurality of benzodiazepines can be prepd. simultaneously.

IT **28920-43-6**, Fluorenylmethoxycarbonyl chloride
RL: RCT (Reactant)
(protection by, of aminobenzophenone deriv., in solid-phase benzodiazepine synthesis)

L94 ANSWER 82 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1994:107617 HCAPLUS
DN 120:107617
TI Synthetic methods for the implementation of encoded **combinatorial chemistry**
AU Nielsen, John; Brenner, Sydney; Janda, Kim D.
CS Dep. Mol. Biol., Scripps Res. Inst., La Jolla, CA, 92037, USA
SO J. Am. Chem. Soc. (**1993**), 115(21), 9812-13
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA English
AB There has been a recent renaissance in drug screening with the development of new technologies which allow a large no. of compds. to be simultaneously exposed to a target. In these "**combinatorial libraries**", compds. that bind to the target with the highest affinity are selected from the pool of statistical sequences. Recently, a scheme for encoding **combinatorially** synthesized **libraries** has been proposed to surmount a no. of the limitations possessed by existing methods. Encoded **combinatorial chem.** combines the large diversity that can be achieved with a **chem. library** with an encoded genetic tag which can be used for the identification and sequential enrichment of any active component. The authors have now developed the **chem.** necessary to implement the conceptual scheme and how a CPG matrix can be appended to allow the parallel synthesis of **peptides** and their encoding

nucleic acid sequences in an alternating, bi-directional manner. In addn. the authors demonstrate how the same support can be modified to permit a controlled "dendritic" display of the **chem. library**. Implementation of this latter regime provides a novel methodol. for controlled multivalent **combinatorial** ligand display.

IT **28920-43-6**, 9-Fluorenylmethyl chloroformate
RL: RCT (Reactant)
(reaction of, in synthesis of DNA)

L94 ANSWER 83 OF 83 HCAPLUS COPYRIGHT 2001 ACS
AN 1994:27026 HCAPLUS
DN 120:27026
TI Encoded **combinatorial chemical libraries**
IN Lerner, Richard; Janda, Kim; Brenner, Sydney; Nielsen, John
PA Scripps Research Institute, USA
SO PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DT **Patent**
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9320242	A1	19931014	WO 1993-US3127	19930330	<--
	W: AU, CA, JP, US					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	US 5573905	A	19961112	US 1992-860445	19920330	<--
	AU 9339449	A1	19931108	AU 1993-39449	19930330	<--
	AU 685050	B2	19980115			
	EP 643778	A1	19950322	EP 1993-908732	19930330	<--
	EP 643778	B1	20000531			
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
	JP 07505530	T2	19950622	JP 1993-517730	19930330	<--
	AT 193561	E	20000615	AT 1993-908732	19930330	<--
	ES 2147197	T3	20000901	ES 1993-908732	19930330	<--
	US 5723598	A	19980303	US 1996-665511	19960618	<--
	US 6060596	A	20000509	US 1998-33743	19980303	<--
PRAI	US 1992-860445	A2	19920330	<--		
	WO 1993-US3127	A	19930330	<--		
	US 1996-665511	A3	19960618	<--		

AB A method of screening synthetic compds. (e.g. series of **peptides**) for biol. (binding, activating, catalytic, etc.) activity involves synthesis of a **library** of bifunctional mols., each comprising a candidate active polymer and an identifying synthetic genetic tag. Two alternating parallel **combinatorial** syntheses are performed, such that addn. of 1 **chem.** unit to the candidate active compd. is followed by addn. of an identifying oligonucleotide sequence; the **library** is built up by repetition of this process. Serial enrichment of active mols. is achieved by PCR amplification of and hybridization with their genetic tag sequences; sequencing the genetic tag identifies the sequence of the active mol. Thus, activated controlled-pore glass was coupled in 2 steps with an aq. NH3-cleavable sarcosine-succinyl-6-aminohexanol linker, and a bifunctional branch monomer, O-(4,4'-dimethoxytrityl)-N-fluorenylmethoxycarbonylserine, was added by amidation of the terminal amino group of aminohexanol. Removal of the dimethoxytrityl group allowed addn. of a blocked nucleotide phosphoramidite, and subsequent removal of the fluorenylmethoxycarbonyl group allowed addn. of a protected **amino acid**; addnl. nucleotide and **amino acid** residues were added alternately. The synthesis included the steps of aliquoting, adding different units to each aliquot, and pooling the aliquots to build the **library** of bifunctional mols. sequentially. PCR primer binding sites may be added as blocks rather than added nucleotide by nucleotide.

IT **28920-43-6**, 9-Fluorenylmethyl chloroformate
RL: ANST (Analytical study)
(condensation of, with aminohexanol)

L32 ANSWER 2 OF 2 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
TI New method for forming a combinatorial library - useful for identifying pharmaceutical and agricultural lead compounds..
AB WO 9835923 A UPAB: 19981028
A new method for forming a combinatorial library comprises: (a) mixing a number of core molecules having at least one reactive centre with a number of different tool molecules having at least one functional group to form a reaction mixture; and (b) reacting the reactive centres of the core molecules with the functional groups of the tool molecules to form a number of library molecules.

USE - The method is useful for preparing a library of non-naturally occurring molecules using a kit which includes instructions for reacting the core molecules and tool molecules to form the library. The libraries are useful for identifying pharmaceutical and agricultural lead compounds.

ADVANTAGE - None given.

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FILE LAST UPDATED: 5 Jun 2001 (20010605/ED)

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=> d 178 all tot

L78 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:8206 HCAPLUS
DN 130:63329
TI **Combinatorial** process for preparing substituted phenylalanine **libraries** for use in assay kits and automated assay machines
IN Heerding, Julia Marie; Lampe, John William
PA Eli Lilly and Company, USA
SO PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM G01N033-53
ICS G01N033-543; G01N033-566; C07C229-00
CC 9-1 (Biochemical Methods)
Section cross-reference(s): 1, 34
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9857173	A1	19981217	WO 1998-US11909	19980610 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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	AU 9880630	A1	19981230	AU 1998-80630	19980610 <--
PRAI	US 1997-49054		19970610 <--		
	WO 1998-US11909		19980610		

OS MARPAT 130:63329
AB This invention relates to a novel diverse **combinatorial library** of substituted phenylalanine compds. and to an app. providing a readily accessible source of individual members of the **library**. The app. can be used in assay kits and as a replaceable element in automated assay machines. Merrifield resin was reacted with

p-nitrophenyl-N-Boc-phenylalanine, the amino-protecting group was removed, and the resin-bound product was acylated. The nitro group was reduced and a second acylation was performed.

ST **combinatorial** substituted phenylalanine **library** assay kit; automated analyzer substituted phenylalanine **combinatorial library**

IT **Acid chlorides (organic)**
RL: RCT (Reactant)
(acylation with; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)

IT Signal transduction (biological)
Transcriptional regulation
(assay kits for cell-based assays for; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)

IT Fluorescence polarization immunoassay
(assay kits for; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)

IT Cell (biological)
(assays based on, assay kits for; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)

IT Analytical apparatus
(automated; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)

IT Biosensors
(calorimetric; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)

IT Acylation
Combinatorial chemistry
Combinatorial library
Drug screening
Test kits
(**combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)

IT Green fluorescent **protein**
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(**combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)

IT Fluorometry
(correlation, assay kits for; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)

IT Sensors
(elec. cell impedance; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)

IT Enzymes, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(endothelin-converting, radioassay, assay kits for; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)

IT Biological materials
(for assay kits; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)

IT Genes (animal)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(for receptors, constructs, for cell-based assays, assay kits for; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)

IT Virus

(infectivity, assay kits for cell-based assays for; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)

IT Enzymes, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(inhibition assays, assay kits for; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)

IT Microtiter plates
(multi-well; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)

IT **Proteins** (general), biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**protein** interaction assays, assay kits for; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)

IT DNA
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**protein**-DNA interaction assays, assay kits for; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)

IT Human immunodeficiency virus
(proteinase of, radio enzyme assay, assay kits for; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)

IT Scintillation
(proximity assays, assay kits for; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)

IT Cholesteryl ester transfer **protein**
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(radioassay, assay kits for; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)

IT **Ligands**
Receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(receptor-**ligand** binding assays, assay kits for; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)

IT Apparatus
(well plate, contg. **library** compds. for drug screening; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)

IT Plates
(well, contg. **library** compds. for drug screening; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)

IT 9001-92-7, Proteinase
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(HIV, radioassay, assay kits for; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)

IT 11128-99-7, Angiotensin II
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(IPA receptor binding assay, assay kits for; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)

IT 75-09-2, Methylene chloride, miscellaneous
RL: MSC (Miscellaneous)
(acylation in org. solvent of; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)

IT 7087-68-5, Diisopropylethylamine 57951-36-7, Dimethylaminopyridine
RL: MSC (Miscellaneous)

(acylation with **acid chloride** in presence of; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)
IT 9014-00-0, Luciferase 9073-60-3, .beta.-Lactamase
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(**combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)
IT 63-91-2DP, Phenylalanine, substituted
RL: ARG (Analytical reagent use); BPR (Biological process); DEV (Device component use); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(**combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)
IT 9003-70-7D, chloromethylated 33305-77-0 61280-75-9 112352-59-7D, **amine**-protected
RL: RCT (Reactant)
(**combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)
IT 86937-80-6DP, Merrifield resin-bound
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(**combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)
IT 584-08-7
RL: MSC (Miscellaneous)
(coupling reaction with solid support in presence of; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)
IT 52930-59-3
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(for cell-based assays, assay kits for; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)
IT 7772-99-8, Tin chloride (SnCl2), reactions
RL: RCT (Reactant)
(nitro group redn. with; **combinatorial** process for prepg. substituted phenylalanine **libraries** for use in assay kits and automated assay machines)
RE.CNT 7
RE
(1) Chugi Seiyaku Kabushiki Kaisha; WO 9618607 A1 1996 HCAPLUS
(2) Degraw, J; J Med Chem 1972, V15(7), P781 HCAPLUS
(3) Gordon; J Med Chem 1994, V37(10), P1385 HCAPLUS
(4) Ouihia, A; Tetrahedron Letters 1992, V33(38), P5509 HCAPLUS
(5) Pfizer Limited; EP 0358398 A1 1990 HCAPLUS
(6) Pfost; US 5104621 A 1992
(7) Searle, G; WO 9736859 A1 1997 HCAPLUS

L78 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:277671 HCAPLUS
DN 128:289517
TI Rapid characterization of **combinatorial libraries** using electrospray ionization Fourier transform ion cyclotron resonance mass spectrometry
AU Fang, A. S.; Vouros, P.; Stacey, C. C.; Kruppa, G. H.; Laukien, F. H.; **Wintner, E. A.**; Carell, T.; Rebek, J., Jr.
CS Department of Chemistry, Barnett Institute, Northeastern University, Boston, MA, 02115, USA
SO Comb. Chem. High Throughput Screening (1998), 1(1), 23-33
CODEN: CCHSFU; ISSN: 1386-2073
PB Bentham Science Publishers
DT Journal
LA English
CC 80-5 (Organic Analytical Chemistry)
Section cross-reference(s): 22
AB The relatively new field of **combinatorial chem.** has

enabled researchers to create large mixts. of compds. that can be screened for leads in developing potential drug candidates. The new synthetic method has also created a need for better procedures to analyze the complex mixts. that are generated. The immediate goal in most cases is to verify the synthetic procedure and to det. the purity and completeness of the **library** sample before binding studies are initiated. The authors report here a method to rapidly characterize small-mol. combining a core mol. bearing two **acid chloride** functionalities with various amino acids to generate **libraries** of 36, 78 and 120 components. Using electrospray ionization Fourier transform ICR mass spectrometry (ESI-FTICR-MS) the authors were able to identify 70-80% of the **library** components. All samples were analyzed as mixts. by direct infusion without chromatog. sepn. Also, nominally isobaric components could be resolved and identified through exact mass assignments without tandem mass spectrometry. ESI-FTICR-MS is a rapid and convenient tool for the characterization of small-mol. **libraries**. The method is esp. useful for the anal. of larger **libraries** that contain many nominally isobaric components and impurities.

ST **combinatorial library** Fourier ICR mass spectrometry; ion cyclotron resonance MS **combinatorial library**

IT **Combinatorial library**
Fourier transform ion cyclotron resonance mass spectrometry
(rapid characterization of **combinatorial libraries** using electrospray ionization Fourier transform ion cyclotron resonance mass spectrometry)

IT 178916-23-9
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(132060265rapid characterization of **combinatorial libraries** using electrospray ionization Fourier transform ion cyclotron resonance mass spectrometry)

IT 616-34-2, Glycine methyl ester 2812-46-6 3017-32-1 4299-70-1, L-Tryptophane methyl ester 10332-17-9, L-Methionine methyl ester 13211-31-9, L-Valine-tert-butyl ester 13795-73-8 16874-06-9 16874-17-2 21691-50-9 21691-53-2, L-Leucine-tert-butyl ester 24205-25-2 25456-86-4, L-Asparagine-tert-butyl ester 35146-32-8 48067-24-9 52616-82-7 80745-10-4
RL: RCT (Reactant)
(building block in rapid characterization of **combinatorial libraries** using electrospray ionization Fourier transform ion cyclotron resonance mass spectrometry)

IT 166034-31-7
RL: RCT (Reactant)
(core mol. in rapid characterization of **combinatorial libraries** using electrospray ionization Fourier transform ion cyclotron resonance mass spectrometry)

IT 178915-00-9 178915-02-1 178915-03-2 178915-04-3 178915-05-4
178915-06-5 178915-07-6 178915-08-7 178915-09-8 178915-10-1
178915-11-2 178915-12-3 178915-13-4 178915-14-5 178915-15-6
178915-16-7 178915-17-8 178915-18-9 178915-19-0 178915-20-3
178915-30-5 178915-31-6 178915-32-7 178915-33-8 178915-34-9
178915-35-0 178915-37-2 178915-38-3 178915-39-4 178915-40-7
178915-41-8 178915-42-9 178915-43-0 178915-45-2 178915-46-3
178915-47-4 178915-48-5 178915-50-9 178915-51-0 178915-52-1
178915-54-3 178915-55-4 178915-56-5 178915-57-6 178915-58-7
178915-59-8 178915-60-1 178915-61-2 178915-62-3 178915-64-5
178915-65-6 178915-66-7 178915-67-8 178915-81-6 178915-83-8
178915-87-2 178915-88-3 178915-92-9 178915-93-0 178915-94-1
178915-95-2 178915-96-3 178915-97-4 178915-98-5 178916-00-2
178916-01-3 178916-02-4 178916-03-5 178916-05-7 178916-06-8
178916-07-9 178916-08-0 178916-09-1 178916-10-4 178916-11-5
178916-12-6 178916-14-8 178916-15-9 178916-16-0 178916-17-1
178916-20-6 178916-21-7 178916-22-8 178916-24-0 178916-25-1
178916-26-2 178916-27-3 178916-29-5 178916-30-8 178916-32-0
178916-35-3 178916-36-4 178916-37-5 178916-39-7 178916-40-0
178916-43-3 178916-45-5 178916-46-6 178916-47-7 178916-48-8
178916-49-9 178916-50-2 178916-52-4 178916-53-5 178916-54-6

205806-37-7 205806-38-8 205806-39-9 205806-40-2 205806-41-3
205806-42-4 205806-43-5 205806-44-6 205806-45-7 205806-46-8
205806-47-9 205806-48-0 205806-49-1 205806-50-4 205806-51-5
205806-52-6 205806-53-7 205806-54-8 205806-55-9 205806-58-2
205806-64-0 205806-67-3 205806-70-8 205806-72-0 205806-74-2
205806-76-4 205806-77-5 205806-78-6 205806-79-7
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(rapid characterization of **combinatorial libraries** using electrospray ionization Fourier transform ion cyclotron resonance mass spectrometry)

L78 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:599851 HCAPLUS
DN 123:102049
TI New promise in **combinatorial chemistry**: Synthesis, characterization, and screening of small-molecule **libraries** in solution
AU Carell, Thomas; **Wintner, Edward A**; Sutherland, Andrew J; Rebek, Julius Jr; Dunayevskiy, Yuriy M; Vouros, Paul
CS Department Chemistry, Massachusetts Institute Technology, Cambridge, MA, 02139, USA
SO Chem. Biol. (1995), 2(3), 171-83
CODEN: CBOLE2; ISSN: 1074-5521
DT Journal
LA English
CC 1-4 (Pharmacology)
AB The increasing interest in **combinatorial chem.** as a tool for the development of therapeutics has led to many new methods of creating mol. **libraries** of potential lead compds. Current methods have made it possible to develop **libraries** of several million compds. As a result, the limiting factor in the screening of **libraries** has become the identification and characterization of active species. The authors have recently described a method for generating **libraries** of water-sol. compds. contg. mixts. of 104 to 105 different small org. mols. by using generally applicable soln. phase **chem.** The authors set out to develop new methods to characterize and decode these **libraries. Libraries** were generated by condensing a multi-**acid-chloride** core mol. with various amines, producing mols. with functional groups about a rigid backbone. Compn. and complexity of the **libraries** was evaluated using electrospray mass spectrometry to analyze model **libraries** contg. .ltoreq.55 different mols. The no. of peaks obtained in mass spectrometry is directly correlated with the complexity of the **library**, and the authors were therefore able to deduce which of the expected compds. had in fact been formed in the **library**, and which of the building blocks in the **library** were not efficiently used. An iterative selection procedure was developed using this information, which allowed the screening of **libraries** of .ltoreq.50,000 **chem.** species to produce a competitive inhibitor of the enzyme trypsin. The authors' strategy for the identification of active species should be broadly applicable to other methods of generating complex **libraries** of small mols. The selection from the **library** of a compd. with desired biol. properties augurs well for the potential value of generating and screening complex mixts. of small mols. in soln.
ST **combinatorial library chem** pharmacol screening; trypsin inhibitor **combinatorial library acid chloride**
IT **Combinatorial library**
Pharmacology
(new promise in **combinatorial chem.** in relation to synthesis and characterization and pharmacol. screening of small-mol. **libraries** in soln. as trypsin inhibitors)
IT 9002-07-7, Trypsin
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(inhibitors; new promise in **combinatorial chem.** in

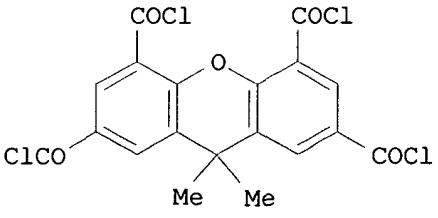
relation to synthesis and characterization and pharmacol. screening of small-mol. **libraries** in soln. as trypsin inhibitors)

IT 77354-22-4D, 1,3,5-Benzenetriacetyl trichloride, derivs. 161980-55-8D, derivs. 165465-27-0D, derivs. 166034-31-7D, derivs. 166034-32-8D, derivs.
RL: BAC (Biological activity or effector, except adverse); PRP (Properties); BIOL (Biological study)
(new promise in **combinatorial chem.** in relation to synthesis and characterization and pharmacol. screening of small-mol. **libraries** in soln. as trypsin inhibitors)

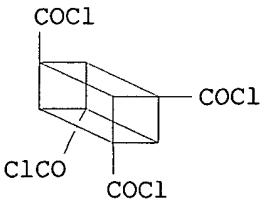
IT 166034-37-3P 166034-38-4P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(new promise in **combinatorial chem.** in relation to synthesis and characterization and pharmacol. screening of small-mol. **libraries** in soln. as trypsin inhibitors)

IT 166034-33-9P 166034-34-0P 166034-35-1P 166034-36-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(new promise in **combinatorial chem.** in relation to synthesis and characterization and pharmacol. screening of small-mol. **libraries** in soln. as trypsin inhibitors)

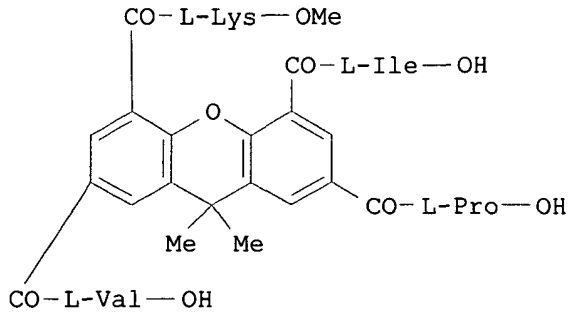
L78 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:542626 HCAPLUS
DN 123:74100
TI Screening method for isolation in solution of biologically active compounds from a molecular **library**
AU Carell, Thomas; **Wintner, Edward A.**; Rebek, Julius Jr.
CS Dep. Chem., Massachusetts Inst. Technol., Cambridge, MA, 02139, USA
SO Angew. Chem. (1994), 106(20), 2162-4 (See also Angew. Chem., Int. Ed. Engl., 1994, 33(20), 2061-4)
CODEN: ANCEAD; ISSN: 0044-8249
DT Journal
LA German
CC 1-1 (Pharmacology)
Section cross-reference(s): 21
GI



I



II



III

AB I and II were condensed with 19 amino acids to produce a **combinatorial library**. A method is described whereby this **library** was screened for trypsin-inhibitory activity. The most active compd. in this assay was III.
ST **combinatorial library** trypsin inhibitor xanthene peptide; cubane peptide trypsin inhibitor **combinatorial library**; peptide cubane xanthene antitrypsin **combinatorial library**
IT Amino acids, biological studies
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reaction products with xanthenetetracarboxylic **acid chloride** or cubanetetracarboxylic **acid chloride**; screening method for isolation in soln. of biol. active compds. from a mol. **library**)
IT **Combinatorial library**
(screening method for isolation in soln. of biol. active compds. from a mol. **library**)
IT 9002-07-7, Trypsin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; screening method for isolation in soln. of biol. active compds. from a mol. **library**)
IT 161980-55-8 165465-27-0 165465-28-1 165465-29-2
RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(reaction products with amino acids; screening method for isolation in soln. of biol. active compds. from a mol. **library**)

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L120 ANSWER 1 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:310596 BIOSIS
DN PREV200000310596
TI Quantized surface complementarity diversity (**QSCD**): A model based on small molecule-target complementarity.
AU **Wintner, Edward A.**; Moallemi, Ciamac C.
SO Journal of Medicinal Chemistry, (May 18, 2000) Vol. 43, No. 10, pp. 1993-2006. print.
ISSN: 0022-2623.
DT Article
LA English
SL English
AB A model of molecular diversity is presented. The model, termed "Quantized Surface Complementarity Diversity" (**QSCD**), defines molecular diversity by measuring molecular complementarity to a fully enumerated set of theoretical target surfaces. Molecular diversity space is defined as the molecular complement to this set of enumerated surfaces. Using a set of known test compounds, the model is shown to be biologically relevant, consistently scoring known actives as similar. At the resolution of the model, which examines molecules "quantized" into 4.24 ANG cubic units and treats four points of specific energetic complementarity, the minimum number of compounds needed to fully cover molecular diversity space up to

volume 1070 cubic ANG is estimated to be on the order of 24 million molecules. Most importantly, **QSCD** allows for individual points in diversity space to be filled by direct modeling of molecular **libraries** into detailed 3D templates of shape and functionality.

CC Pharmacology - General *22002
General Biology - Information, Documentation, Retrieval and Computer Applications *00530
Biochemical Methods - General *10050
Biochemical Studies - General *10060
Biophysics - Molecular Properties and Macromolecules *10506

IT Major Concepts
Computer Applications (Computational Biology); Pharmacology

IT Chemicals & Biochemicals
molecule: pharmaceutical

IT Methods & Equipment
quantized surface complementarity diversity: analytical method, computer method

IT Miscellaneous Descriptors
drug development; molecular complementarity; molecular diversity; molecular **library**

L120 ANSWER 2 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1999:145228 BIOSIS
DN PREV199900145228
TI Process for creating molecular diversity and novel protease inhibitors produced thereby.
AU Rebek, J., Jr.; Carell, T.; **Wintner, E. A.**
CS 100 Memorial Dr., #5-3A, Cambridge, Mass. 02142 USA
PI US 5877030 March 2, 1999
SO Official Gazette of the United States Patent and Trademark Office Patents, (March 2, 1999) Vol. 1220, No. 1, pp. 495.
ISSN: 0098-1133.
DT Patent
LA English
NCL 436518000

IT Major Concepts
Biochemistry and Molecular Biophysics; Enzymology (Biochemistry and Molecular Biophysics); Methods and Techniques; Pharmacology

IT Industry
chemical industry

IT Miscellaneous Descriptors
COMBINATORIAL LIBRARY; CREATION METHODS; MOLECULAR DIVERSITY; NOVEL PROTEASE INHIBITORS; PHARMACEUTICALS

L120 ANSWER 3 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1998:280891 BIOSIS
DN PREV199800280891
TI **Combinatorial libraries** in solution: Polyfunctionalized core molecules.
AU **Wintner, Edward A.**; Rebek, Julius, Jr.
CS Skaggs Inst. Chem. Biol., The Scripps Res. Inst., La Jolla, CA 92037 USA
SO Wilson, S. R. [Editor]; Czarnik, A. W. [Editor]. (1997) pp. 95-117. Combinatorial chemistry: Synthesis and application.
Publisher: John Wiley and Sons, Inc. 605 Third Avenue, New York, New York 10158-0012, USA.
ISBN: 0-471-12687-X.
DT **Book**
LA English
CC Pharmacology - General *22002
Biochemical Methods - General *10050
Biochemical Methods - Proteins, Peptides and Amino Acids *10054
Biochemical Studies - General *10060
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - General Biophysical Techniques *10504
Biophysics - Molecular Properties and Macromolecules *10506
Enzymes - Methods *10804

IT Major Concepts
Methods and Techniques; Pharmacology
IT Chemicals & Biochemicals
peptide: synthesis; polyfunctionalized molecule: analysis, potential therapeutic agent, synthesis
IT Methods & Equipment
combinatorial method: synthetic method; electrospray ionization mass spectrometry: analytical method; enzymatic **screening** method: analytical method
IT Miscellaneous Descriptors
combinatorial library: analysis, synthesis, **screening; Book** Chapter

L120 ANSWER 4 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1998:205614 BIOSIS
DN PREV199800205614
TI The activated core approach to **combinatorial chemistry** : A selection of new core molecules.
AU Pryor, Kent E.; **Shipps, Gerald W., Jr.**; Skyler, David A.; Rebek, Julius, Jr. (1)
CS (1) Skaggs Inst. Chem. Biol., La Jolla, CA 92037 USA
SO Tetrahedron, (April 16, 1998) Vol. 54, No. 16, pp. 4107-4124. ISSN: 0040-4020.
DT Article
LA English
AB Four new activated core molecules suitable for use in solution-phase **combinatorial** organic **chemistry** have been prepared. These molecules represent an attempt to further explore shape-space and increase the structural diversity of prepared **libraries**, as well as to incorporate recognition elements in the cores to increase the chances for interaction with biological targets. Demonstrations of deconvolution strategies used to simplify complex **libraries** and build individual molecular species based on the cores are also provided.
CC Biochemical Methods - General *10050
Biochemical Studies - General *10060
IT Major Concepts
Biochemistry and Molecular Biophysics
IT Chemicals & Biochemicals
core molecules
IT Miscellaneous Descriptors
activated core approach; **combinatorial chemistry**; shape-space; structural diversity

L120 ANSWER 5 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1998:493 BIOSIS
DN PREV199800000493
TI Synthesis and **screening** of small molecule **libraries** active in binding to DNA.
AU **Shipps, Gerald W., Jr.**; Pryor, Kent E.; Xian, Jun; Skyler, David A.; Davidson, Eric H.; Rebek, Julius, Jr. (1)
CS (1) Scripps Res. Inst., 10550 North Torrey Pines Rd., MB-26, La Jolla, CA 92037 USA
SO **Proceedings of the National Academy of Sciences of the United States of America**, (Oct. 28, 1997) Vol. 94, No. 22, pp. 11833-11838. ISSN: 0027-8424.
DT Article
LA English
AB Five synthetic **combinatorial libraries** of 2,080 components each were **screened** as mixtures for inhibition of DNA binding to two transcription factors. Rapid, solution-phase synthesis coupled to a gel-shift assay led to the identification of two compounds active at a 5- to 10-muM concentration level. The likely mode of inhibition is intercalation between DNA base pairs. The efficient deconvolution through sublibrary synthesis augurs well for the use of large mixtures of small, nonpeptide molecules in biological **screens**.

CC Biochemical Methods - General *10050
Genetics and Cytogenetics - General *03502
Biochemical Studies - General *10060
Biochemical Studies - Nucleic Acids, Purines and Pyrimidines *10062
Biophysics - Molecular Properties and Macromolecules *10506
IT Major Concepts
Biochemistry and Molecular Biophysics
IT Chemicals & Biochemicals
small nonpeptide molecules: DNA binding, synthesis; DNA
IT Methods & Equipment
gel shift assay: analytical method; rapid solution phase synthesis: synthetic method

L120 ANSWER 6 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1996:327104 BIOSIS
DN PREV199699049460
TI Application of capillary electrophoresis-electrospray ionization mass spectrometry in the determination of molecular diversity.
AU Dunayevsky, Yuriy M.; Vouros, Paul (1); **Wintner, Edward A.**; **Shipps, Gerald W.**; Carell, Thomas; Rebek, Julius, Jr.
CS (1) Dep. Chem., Barnett Inst., Northeast. Univ., Boston, MA 02115 USA
SO **Proceedings of the National Academy of Sciences of the United States of America**, (1996) Vol. 93, No. 12, pp. 6152-6157.
ISSN: 0027-8424.
DT Article
LA English
AB By means of capillary electrophoresis coupled online to electrospray ionization MS, a **library** of theoretically 171 disubstituted xanthene derivatives was analyzed. The method allowed the purity and makeup of the **library** to be determined: 160 of the expected compounds were found to be present, and 12 side-products were also detected in the mixture. Due to the ability of capillary electrophoresis to separate analytes on the basis of charge, most of the xanthene derivatives could be resolved by simple capillary electrophoresis-MS procedures even though 124 of the 171 theoretical compounds were isobaric with at least one other molecule in the mixture. Any remaining unresolved peaks were resolved by MS/MS experiments. The method shows promise for the analysis of small **combinatorial libraries** with fewer than 1000 components.
CC Biochemical Methods - General *10050
Biochemical Studies - General *10060
Biophysics - General Biophysical Techniques *10504
Biophysics - Molecular Properties and Macromolecules *10506
IT Major Concepts
Biochemistry and Molecular Biophysics; Methods and Techniques
IT Miscellaneous Descriptors
ANALYTICAL METHOD; CHARGE

L120 ANSWER 7 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1996:273542 BIOSIS
DN PREV199698829671
TI Affinity-based **screening** of **combinatorial libraries** using automated, serial-column chromatography.
AU Evans, David M.; Williams, Kevin P.; McGuinness, Brian; Tarr, George; Regnier, Fred; Afeyan, Noubar; **Jindal, Satish (1)**
CS (1) PerSeptive Biosystems, 500 Old Connecticut Path, Framingham, MA 01701 USA
SO Nature Biotechnology, (1996) Vol. 14, No. 4, pp. 504-507.
ISSN: 1087-0156.
DT Article
LA English
AB We have developed an automated serial chromatographic technique for **screening** a **library** of compounds based upon their relative affinity for a target molecule. A "target" column containing the immobilized target molecule is set in tandem with a reversed-phase column. A **combinatorial** peptide **library** is injected onto the

target column. The target-bound peptides are eluted from the first column and transferred automatically to the reversed-phase column. The target-specific peptide peaks from the reversed phase column are identified and sequenced. Using a monoclonal antibody (3E-7) against beta-endorphin as a target, we selected a single peptide with sequence YGGFL from approximately 5800 peptides present in a **combinatorial library**. We demonstrated the applicability of the technology towards selection of peptides with predetermined affinity for bacterial lipopolysaccharide (LPS, endotoxin). We expect that this technology will have broad applications for **high throughput screening** of **chemical libraries** or natural product extracts.

CC Genetics and Cytogenetics - General *03502
Comparative Biochemistry, General *10010
Biochemical Methods - General *10050
Biochemical Methods - Proteins, Peptides and Amino Acids *10054
Biochemical Studies - General *10060
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biochemical Studies - Lipids *10066
Biochemical Studies - Carbohydrates *10068
Biophysics - General Biophysical Techniques *10504
Biophysics - Molecular Properties and Macromolecules *10506
Biophysics - Bioengineering *10511
Pathology, General and Miscellaneous - Therapy *12512
Endocrine System - Pituitary *17014
Endocrine System - Neuroendocrinology *17020
Pharmacology - General *22002
Pharmacology - Clinical Pharmacology *22005
Toxicology - General; Methods and Experimental *22501
Physiology and Biochemistry of Bacteria *31000
Immunology and Immunochemistry - General; Methods *34502

IT Major Concepts
Biochemistry and Molecular Biophysics; Endocrine System (Chemical Coordination and Homeostasis); General Life Studies; Genetics; Immune System (Chemical Coordination and Homeostasis); Methods and Techniques; Pathology; Pharmacology; Physiology; Toxicology

IT Chemicals & Biochemicals
BETA ENDORPHIN

IT Sequence Data
peptide sequence

IT Miscellaneous Descriptors
ANALYTICAL METHOD; AUTOMATION; BACTERIAL LIPOPOLYSACCHARIDE; BETA ENDORPHIN; BIOTECHNOLOGY; BROAD APPLICATIONS; CHEMICAL **LIBRARIES**; DRUGS; ENDOTOXIN; GENETIC ENGINEERING; IMMOBILIZED TARGET MOLECULE; MONOCLONAL ANTIBODY; NATURAL PRODUCT EXTRACTS; PHARMACEUTICALS; THERAPEUTICS

RN 60617-12-1 (BETA ENDORPHIN)

L120 ANSWER 8 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1995:422867 BIOSIS
DN PREV199598437167
TI Efficient generation of tetraurea **libraries** on a rigid core.
AU **Shipps, G. W.**; Spitz, U. P.; Rebek, J., Jr.
CS Dep. Chem., Mass. Inst. Technol., Cambridge, MA 02139 USA
SO Abstracts of Papers American Chemical Society, (1995) Vol. 210, No. 1-2, pp. ORGN 342.
Meeting Info.: **210th American Chemical Society National Meeting** Chicago, Illinois, USA August 20-24, 1995
ISSN: 0065-7727.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Methods - General *10050
Biochemical Methods - Proteins, Peptides and Amino Acids *10054
Biochemical Studies - General *10060

Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - Molecular Properties and Macromolecules *10506
IT Major Concepts
Biochemistry and Molecular Biophysics; Methods and Techniques
IT Chemicals & Biochemicals
XANTHENE
IT Miscellaneous Descriptors
AMINO ACID METHYL ESTER GROUP; **MEETING ABSTRACT**;
SYNTHETIC METHOD; XANTHENE
RN 92-83-1 (XANTHENE)

L120 ANSWER 9 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1995:403304 BIOSIS
DN PREV199598417604
TI A Tandem-Column Chromatographic Method for Studying the Interaction between Ligands and Their Targets: Lipopolysaccharide as a Model.
AU Evans, David M.; Williams, Kevn P.; Parsons, George; **Jindal, Satish (1)**
CS (1) PerSeptive Biosyst., 500 Old Connecticut Path, Framingham, MA 01701 USA
SO Analytical Biochemistry, (1995) Vol. 229, No. 1, pp. 42-47.
ISSN: 0003-2697.
DT Article
LA English
AB The identification of a lead ligand from a **library** of compounds for a specific target requires both a selection process and a method to assess relative affinities. Using a tandem-column chromatographic technique, we have developed a novel and rapid method for determination of relative affinities for ligands binding to a specific target molecule. We demonstrate, using known ligands for the lipid A region of lipopolysaccharide, that the relative affinities of these ligands can be determined and may be used to characterize the competitive interaction between ligands for the same target. The method can be adapted toward **screening** of soluble **libraries** of peptides and small molecules and those ligands exhibiting a desired affinity can be rapidly selected for further characterization/development.
CC Mathematical Biology and Statistical Methods *04500
Biochemical Methods - General *10050
Biochemical Methods - Lipids *10056
Biochemical Methods - Carbohydrates *10058
Biochemical Studies - Lipids 10066
Biochemical Studies - Carbohydrates 10068
Biophysics - General Biophysical Techniques *10504
IT Major Concepts
Mathematical Biology (Computational Biology); Methods and Techniques
IT Miscellaneous Descriptors
AFFINITY; ANALYTICAL METHOD; MATHEMATICAL MODEL

L120 ANSWER 10 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1995:50743 BIOSIS
DN PREV199598065043
TI A biophysical study of integral membrane **protein folding**.
AU Hunt, J. F.; **Kalghatgi, K.**; Horvath, C.; Rothschild, K. J.; Engelman, D. M.
CS Yale Univ., New Haven, CT 06520 USA
SO Molecular Biology of the Cell, (1994) Vol. 5, No. SUPPL., pp. 8A.
Meeting Info.: **Thirty-fourth Annual Meeting of the American Society for Cell Biology** San Francisco, California, USA December 10-14, 1994
ISSN: 1059-1524.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biophysics - Molecular Properties and Macromolecules 10506

Biophysics - Membrane Phenomena *10508
Physiology and Biochemistry of Bacteria *31000
Genetics of Bacteria and Viruses *31500
BC Bacteria - General Unspecified *05000
IT Major Concepts
Genetics; Membranes (Cell Biology); Physiology
IT Miscellaneous Descriptors
ALPHA HELIX; BACTERIORHODOPSIN; **MEETING ABSTRACT**; MOLECULAR BIOLOGY; PROTEIN **ASSEMBLY**; THERMODYNAMICS
ORGN Super Taxa
Bacteria - General Unspecified: Eubacteria, Bacteria
ORGN Organism Name
bacteria (Bacteria - General Unspecified)
ORGN Organism Superterms
bacteria; eubacteria; microorganisms

L120 ANSWER 11 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1993:222356 BIOSIS
DN PREV199344106856
TI A biophysical study of integral membrane **protein folding**
.
AU Hunt, John F. (1); Bousche, Olaf (1); **Kalghatgi, Krishna (1)**; Reilly, Karlyne (1); Horvath, Csaba (1); Rothschild, Kenneth J.; Engelman, Donald M. (1)
CS (1) Yale Univ., New Haven, CT USA
SO Biophysical Journal, (1993) Vol. 64, No. 2 PART 2, pp. A124.
Meeting Info.: **Thirty-seventh Annual Meeting of the Biophysical Society** Washington, D.C., USA February 14-18, 1993
ISSN: 0006-3495.
DT **Conference**
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Cytology and Cytochemistry - General *02502
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biophysics - General Biophysical Studies *10502
Biophysics - Molecular Properties and Macromolecules 10506
Biophysics - Membrane Phenomena *10508
BC *00500
IT Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology; Membranes (Cell Biology)
IT Miscellaneous Descriptors
ABSTRACT; SPECTROSCOPY; THERMODYNAMICS
ORGN Organism Name
organisms (Organisms - Unspecified)

L120 ANSWER 12 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1992:365094 BIOSIS
DN BA94:47144
TI **PEPTIDE SCREENING.**
AU **BIRNBAUM S**; MOSBACH K
CS DEP. PURE AND APPLIED BIOCHEM., CHEMICAL CENT., PO BOX 124, UNIV. LUND, S-22100 LUND, LUND, SWED.
SO CURR OPIN BIOTECHNOL, (1992) 3 (1), 49-54.
CODEN: CUOBE3.
FS BA; OLD
LA English
AB Since late 1990, there have been several advances in preparing and **screening** large numbers of various peptides. Developments have continued in methods of **peptide screening** based on peptides exposition on coat proteins, produced via fusion coliphage constructs. Further developments have been made in increasing the multitude of peptides produced by the chemical synthetic strategy, including light-directed, spatially addressable chemical synthesis, single-bead, single-peptide synthesis, as well as iterative peptide

selection and synthesis.
CC Biochemical Methods - Proteins, Peptides and Amino Acids *10054
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Genetics of Bacteria and Viruses *31500
Virology - General; Methods *33502
BC Viruses - Unspecified 02000
IT Miscellaneous Descriptors
REVIEW SOLID PHASE CHEMISTRY CHEMICAL SYNTHESIS SYNTHETIC METHOD FUSION PHAGE PEPTIDE **LIBRARIES** ANALYTICAL METHOD

L120 ANSWER 13 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1992:201727 BIOSIS
DN BR42:94802
TI IMPROVED **RPC** OF HYDROPHOBIC POLYPEPTIDES.
AU HUNT J F; MYERS K; ENGELMAN D M; HORVATH C; **KALGHATGI K**
CS YALE UNIV., NEW HAVEN, CONN.
SO JOINT ANNUAL **MEETING** OF THE BIOPHYSICAL SOCIETY AND THE AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY, HOUSTON, TEXAS, USA, FEBRUARY 9-13, 1992. BIOPHYS J. (1992) 61 (2 PART 2), A90.
CODEN: BIOJAU. ISSN: 0006-3495.
DT **Conference**
FS BR; OLD
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Methods - Proteins, Peptides and Amino Acids *10054
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - General Biophysical Techniques *10504
Biophysics - Molecular Properties and Macromolecules *10506
Biophysics - Membrane Phenomena *10508
IT Miscellaneous Descriptors
ABSTRACT MEMBRANE REVERSED PHASE CHROMATOGRAPHY ANALYTICAL METHOD

L120 ANSWER 14 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1992:156473 BIOSIS
DN BR42:72673
TI IMPROVED **RPC** OF HYDROPHOBIC POLYPEPTIDES.
AU HUNT J F; MYERS K; ENGELMAN D M; HORVATH C; **KALGHATGI K**
CS YALE UNIV., NEW HAVEN, CONN.
SO JOINT **MEETING** OF THE AMERICAN SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY/BIOPHYSICAL SOCIETY, HOUSTON, TEXAS, USA, FEBRUARY 9-13, 1992. FASEB (FED AM SOC EXP BIOL) J. (1992) 6 (1), A90.
CODEN: FAJOEC. ISSN: 0892-6638.
DT **Conference**
FS BR; OLD
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Methods - Proteins, Peptides and Amino Acids *10054
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - General Biophysical Techniques *10504
Metabolism - Proteins, Peptides and Amino Acids *13012
IT Miscellaneous Descriptors
ABSTRACT POLYPEPTIDE AGGREGATION ANALYTICAL METHOD REVERSED PHASE CHROMATOGRAPHY

L120 ANSWER 15 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1989:488091 BIOSIS
DN BR37:109210
TI RAPID **PEPTIDE MAPPING** AND PROTEIN ANALYSIS BY HPLC.
AU **KALGHATGI K**; HORVATH C
CS DEP. CHEM. ENG., YALE UNIV., NEW HAVEN, CONN. 06520, USA.
SO WITTMANN-LIEBOLD, B. (ED.). METHODS IN PROTEIN SEQUENCE ANALYSIS; 7TH INTERNATIONAL **CONFERENCE**, BERLIN, WEST GERMANY, JULY 3-8, 1988. XXXV+575P. SPRINGER-VERLAG NEW YORK, INC: SECUACUS, NEW JERSEY, USA;

BERLIN, WEST GERMANY. ILLUS. (1989) 0 (0), 248-255.
ISBN: 0-387-19433-9, 3-540-19433-9.
FS BR; OLD
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Biochemical Methods - Proteins, Peptides and Amino Acids *10054
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - General Biophysical Techniques 10504
IT Miscellaneous Descriptors
HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY MOLECULAR SEQUENCE DATA PROTEIN SEQUENCE PEPTIDE SEQUENCE

L120 ANSWER 16 OF 16 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1988:498109 BIOSIS
DN BR35:116944
TI RAPID **PEPTIDE MAPPING** BY HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY.
AU **KALGHATGI K**; HORVATH C
CS DEP. CHEM. ENGINEERING, YALE UNIV., P.O. BOX 2159, NEW HAVEN, CT 06520, USA.
SO 7TH INTERNATIONAL **SYMPOSIUM** ON HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY OF PROTEINS, PEPTIDES AND POLYNUCLEOTIDES, PART I, WASHINGTON, D.C., USA, NOVEMBER 2-4, 1987. J CHROMATOGR. (1988) 443 (0), 343-354.
CODEN: JOCRAM. ISSN: 0021-9673.
FS BR; OLD
LA English
CC **General Biology - Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals 00520**
Comparative Biochemistry, General 10010
Biochemical Methods - Proteins, Peptides and Amino Acids *10054
Biochemical Methods - Porphyrins and Bile Pigments 10055
Biochemical Methods - Carbohydrates 10058
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biochemical Studies - Porphyrins and Bile Pigments 10065
Biochemical Studies - Carbohydrates 10068
Biophysics - General Biophysical Techniques *10504
Enzymes - General and Comparative Studies; Coenzymes *10802
Enzymes - Methods *10804
BC Galliformes 85536
Bovidae 85715
Equidae 86145
IT Miscellaneous Descriptors
HORSE CHICKEN BOVINE BETA LACTOGLOBULINS CYTOCHROME C LYSOZYME
RN 9001-63-2 (LYSOZYME)
9007-43-6 (CYTOCHROME C)

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(FILE 'HOME' ENTERED AT 06:47:12 ON 06 JUN 2001)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 06:47:54 ON 06 JUN 2001
E US6207861/PN
L1 1 S E3
E NEOGEN/PA,CS
L2 11 S E13-E20
E NASH H/AU
L3 17 S E3,E25-E27
E BIRNBAUM S/AU
L4 28 S E3-E7,E10,E11

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                E WINTNER E/AU
L5           77 S E3-E8
                E KALGHATGI K/AU
L6           30 S E3-E6
                E SHIPPS G/AU
L7           11 S E4-E8
                E JINDAL S/AU
L8           60 S E3-E7,E13
                E COMBINATORIAL LIBRARY/CT
                E E2+ALL
L9         1243 S E3+NE
                E E4+ALL
L10        4800 S E1+NT
                E E7+ALL
L11        1941 S E2,E3,E1+NT
                E COMBINATORIAL LIBRARY/CT
                E E2+ALL
                E E5+ALL
L12        3289 S E3+NT
                E E12+ALL
L13       12577 S E2,E1+NT
                E E7+ALL
                E E13+ALL
L14        3289 S E11+NT
L15        1675 S E5+NT
L16          16 S L9-L15 AND L2-L8
L17          17 S L2-L8 AND COMBINATOR?(L)(LIBRARY OR CHEM?)
L18          18 S L16,L17
L19           2 S L18 NOT L16
                E NEOMORPH
L20           6 S  E3
L21           1 S L2-L8 AND L20
L22          18 S L18,L19,L21
                E MOLECULAR WEIGHT/CT
                E E3+ALL
L23       11763 S E8,E7
L24      493987 S MOLECULAR () (WEIGHT OR MASS OR SIZE)
L25         499 S L9-L15 AND L24
L26          25 S L9-L15 AND L23
L27         183 S L23,L24 AND COMBINATOR? (L) (LIBRARY OR CHEM?)
                E SCREEN/CT
                E E15+ALL
L28        6116 S E1
                E E2+ALL
L29        6461 S E1
L30        3289 S E7+NT
L31         793 S L28-L30 AND COMBINATOR? (L) (LIBRARY OR CHEM?)
L32         282 S L28-L30 AND L9
L33         615 S L28-L30 AND L10
L34         148 S L28-L30 AND L11
L35        1506 S L25-L27,L31-L34
L36          45 S L35 AND PRECURS?
L37          10 S L35 AND PERIPHER?
L38          53 S L36,L37
L39           3 S L2-L8 AND L35
L40           8 S L2-L8 AND L23-L38
L41          22 S L22,L39,L40
L42          22 S  L1,L41
L43           4 S L42 AND (4/SC OR (RABBIT OR SOLANI)/TI)
L44          18 S L42 NOT L43
L45           6 S L2-L8 AND LIBRARY NOT L41,L44
L46          24 S L44,L45
L47          20 S L46 AND (PEPTIDE OR AMINOACID OR AMINO ACID OR PROTEIN OR SCR
L48          24 S L46,L47
L49         600 S L35 AND (PD<=19980217 OR PRD<=19980217 OR AD<=19980217 OR PY<
L50          20 S L38 AND L49
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L51          19 S L50 NOT L48
L52           7 S L51 AND COMBINATOR?/CW
L53         107 S L49 AND LIGAND
L54          81 S L53 AND (PROTEIN OR AMINO ACID OR AMINOACID OR PEPTIDE OR POL
L55           7 S L53 AND (AMINE OR POLYAMINE OR AMIDE OR POLYAMIDE)
L56          82 S L53 AND L54,L55
L57          70 S L56 AND (LIBRARY OR COMBINATOR?)
L58          12 S L56 NOT L57
L59          37 S L57 AND COMBINATOR?/CW
L60          33 S L57 NOT L48,L52,L59
L61          24 S L60 AND SCREEN?
L62          24 S L61 AND LIBRARY
L63           9 S L60 NOT L61
L64           8 S L63 NOT NS3
L65          49 S L52,L59,L52,L64

     FILE 'HCAPLUS' ENTERED AT 08:56:11 ON 06 JUN 2001
L66       31489 S ACID()(CHLORIDE OR HALIDE)
                E ACID HALIDE/CT
                E E4+ALL
L67        2124 S E37-E41
L68          86 S E4
L69       85008 S E3+NT
L70      108146 S L66-L69
L71         339 S L9-L15 AND L70
L72         228 S COMBINATOR?(L)(LIBRARY OR CHEM?) AND L70
L73         268 S LIBRARY AND L70
L74         420 S L71-L73
L75           3 S L74 AND L2-L8
L76           3 S L74 AND L75
L77           1 S L74 AND L65
L78           4 S L75-L77
L79         258 S L74 AND (PD<=19980217 OR PRD<=19980217 OR AD<=19980217 OR PY<
L80          10 S L79 AND L23,L24
                SEL DN 9 10
L81           2 S E1-E2
L82           4 S L79 AND HIGH()(THROUGHPUT OR THROUGH PUT)
L83          78 S L79 AND (POLYAMINE OR POLYAMIDE OR AMINE OR AMIDE OR POLY()(A
L84          78 S L79 AND (PROTEIN OR PEPTIDE OR POLYPEPTIDE OR AMINO ACID)
L85         127 S L81-L84 NOT L48,L65
L86          70 S L85 AND P/DT
L87          57 S L85 NOT L86
L88          30 S L87 AND COMBINATOR?/CW,TI
L89          51 S L86 AND COMBINATOR?/CW,TI
L90          19 S L86 NOT L89
L91           1 S L90 AND PILOT
L92          87 S L78,L82,L88,L89,L91
L93          83 S L92 NOT L48,L65
L94          83 S L93 NOT L78

     FILE 'HCAPLUS' ENTERED AT 09:15:23 ON 06 JUN 2001

     FILE 'BIOSIS' ENTERED AT 09:16:37 ON 06 JUN 2001
                E NASH H/AU
L95          28 S E3,E17,E18
                E BIRNBAUM S/AU
L96          96 S E3-E12
                E WINTNER E/AU
L97           6 S E4,E5
                E KALGHATGI K/AU
L98          31 S E3-E5
                E SHIPPS G/AU
L99           6 S E4-E7
                E JINDAL S/AU
L100        202 S E3-E8,E12
                E NEOGEN/CS
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L101        367 S L95-100
L102         13 S L101 AND (COMBINATOR? (L) (LIBRARY OR CHEM?) OR HIGH()(THROUG
L103          8 S L102 NOT (DAIRY OR HSP60 OR TROPICS OR SEEDLINGS OR POTENTIAL
L104         87 S L101 AND (00520/CC OR CONFERENCE/DT)
L105        103 S L101 AND (CONGRESS OR CONFERENCE OR POSTER OR SYMPOS? OR MEET
L106          4 S L103 AND L104,L105
L107         17 S L105 NOT L104
L108          4 S L107 AND L106
L109          1 S L107 AND PEPTIDE SCREENING
L110          8 S L103,L106,L108,L109
L111         86 S L104 AND L105
L112         86 S L111 NOT L110
L113          7 S L112 AND (PEPTIDE MAPPING OR PROTEIN FOLDING OR RPC OR LIBRAR
L114         15 S L110,L113
L115         12 S L101 AND LIBRARY
L116          9 S L115 AND L114
L117         15 S L114,L116
L118          3 S L115 NOT L117
L119          1 S L118 AND QSCD
L120         16 S L117,L119

     FILE 'BIOSIS' ENTERED AT 09:28:02 ON 06 JUN 2001
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